The New England
Journal of Medicine

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Volume 239 SEPTEMBER 9, 1948 Number 11

TRANSTRACHEAL ANESTHESIA FOR BRONCHOSCOPY

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BRONCHOSCOPY contributes greatly to the diagnosis and treatment of intrathoracic disease. It is at once apparent that proper anesthesia serves the interest of both the bronchoscopist and the patient.

In a search for the most satisfactory anesthetic technic, the various methods of administering topical agents have been explored, the gamut of general anesthetics has been run, and a series of bronchoscopic and esophagoscopic examinations have been conducted under bilateral vagus-nerve block. The technic described below appears to us to serve best the patient and bronchoscopist. The safety of this method is adequately established by experience with more than 1000 patients given tracheobronchial anesthetics.

For many years in the clinic of the late Tudor Edwards at the Brompton Hospital in England, it has been the custom to inject 5 minims of 20 per cent cocaine solution by means of a needle through the skin and cricothyroid membrane into the trachea.[1] This has been used both in bronchography and bronchoscopy. The technic that we have evolved is based on this maneuver but appears to us to have three advantages. The first advantage is derived from a large quantity of dilute agent that gives more complete surface coverage. The second depends on the administration of this agent in two injections, thus producing anesthesia of the main bronchi as well as the trachea. The final advantage accrues from the fact that the patient is in the dorsal decubitus position during the injection.

The simple equipment is illustrated in Figure 1.

PROCEDURE

The preoperative medication consists of 0.09 gm. of pentobarbital sodium by mouth one and a half hours before bronchoscopy and 0.06 gm. of codeine sulfate by mouth one hour before the procedure.

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Ten or fifteen minutes before the intratracheal anesthetic is administered, the lips, mouth and pharynx of the patient are sprayed with 2 per cent pontocaine hydrochloride (dimethylaminoethyl–p–N–butylaminobenzoate) by means of an ordinary atomizer. This means that approximately 3 minims of 2 per cent solution is administered in three

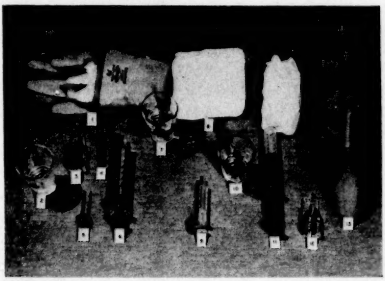

FIGURE 1. *Equipment Used for Transtracheal Anesthesia. (1) Gloves. (2) Saline medicine glass. (3) Ampoules of pontocaine. (4) File. (5) Two 18-gauge needles. (6) Syringe for pontocaine. (7) Alcohol medicine glass. (8) Gauze squares. (9) Syringe for procaine with hypodermic needle. (10) Procaine medicine glass. (11) Syringe for sodium phenobarbital. (12) Ampoules of epinephrine and caffeine sodium benzoate. (13) Pontocaine atomizer.*

sprays to the zones indicated. The patient is instructed to inspire deeply as the nebulizer is directed toward the back of the tongue and oropharynx.

Next, under aseptic technic, with the patient on his back and the head hyperextended, the anterior aspect of the neck is cleansed with 70 per cent alcohol. The cricothyroid membrane is identified with the gloved finger in the midline, between the cricoid and thyroid cartilages (Fig. 2). The skin and subcutaneous tissues are infiltrated with 2-cc. of 2 per cent procaine hydrochloride. Two 2-cc. ampoules of sterile pontocaine hydrochloride,

each containing 20 mg. of the agent, are opened, and 3 cc. of this solution is diluted with 6 cc. of sterile isotonic saline solution. This provides 9 cc. of a 0.3 per cent pontocaine solution and is aspirated into a 10-cc. syringe, through an 18-gauge needle. The needle is then directed through the skin in the infiltrated zone, and through the cricothyroid membrane into the trachea. The intratracheal position of the tip of the needle is verified by the aspiration of air into the syringe. Half of the solution is then quickly injected into the trachea, and the needle is immediately withdrawn. An alcohol sponge is firmly pressed over the injection site, for the patient will immediately cough. With the firm

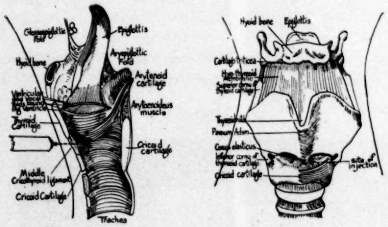

FIGURE 2. *Sagittal and Ventral Aspects of the Laryngeal Anatomy, to Illustrate the Site of Injection.*

pressure maintained, the patient is at once instructed to sit up, and coughing is again encouraged. Tracheal secretions are coughed into an emesis basin. The patient is then returned to the dorsal decubitus position and allowed to remain at rest for approximately five minutes. This recess serves three purposes: it allows time for the agent to anesthetize the upper respiratory tract; an opportunity is afforded to explain the subjective symptoms of bronchoscopic anesthesia and examination (it is essential that the patient be reassured that although he has no sensation of air passing in and out of the trachea and pharynx he is actually breathing adequately); and finally, this interval provides an opportunity to watch the patient for drug toxicity or idiosyncrasy. As a safeguard against such a susceptibility 0.5 gm. of sodium phenobarbital in 10 cc. of water should be available in a syringe ready for intravenous administration. In addition, epinephrine and caffeine sodium benzoate should be at hand in the event of cardiac or respiratory failure. Of course, oxygen should be immediately available in the operating room. Actually, under the outlined conditions, the dangers are virtually negligible.

In a second tracheal injection similar to the first, the remainder of the dilute pontocaine solution (4.5 cc.) is instilled through the cricothyroid membrane. Again, the alcohol pressure sponge is placed over the injection site, the patient is raised to a sitting position, leaned toward the side of principal disease and again instructed to cough. Generally, it has been found that anesthesia is fairly complete throughout the trachea down to the carina, and the patient must be encouraged to cough and expectorate the agent. He is then returned to the dorsal decubitus position and is ready for the bronchoscopic procedure.

After bronchoscopy, the patient is allowed nothing by mouth for three hours lest he aspirate material into the anesthetized tracheobronchial tree.

Discussion

In view of the small quantity of pontocaine employed (30 mg.), the danger of overdosage is probably more theoretical than real; however, sensitivity is possible, since a reaction to four drops of 0.5 per cent pontocaine solution has been reported. Pentobarbital sodium is used in the preoperative medication for prophylaxis against pontocaine reactions. Barbiturates appear to increase tolerance to the anesthetic agent, without reducing efficiency, and their employment before pontocaine anesthesia for bronchoscopy is advised. In addition, it has seemed well to have immediately available a quick-acting barbiturate for intravenous use — 0.5 gm. of sodium phenobarbital in a 10-cc. solution seems adequate for this purpose.

The anesthetic agent is obtained in the form of ampoules of pontocaine hydrochloride, 1 per cent solution (20 mg. in 2 cc.), prepared for spinal anesthesia. Three cubic centimeters of this solution diluted with 6 cc. of isotonic saline solution provides 9 cc. of 0.3 per cent solution, which is adequate for tracheobronchial anesthesia. We believe that the large volume of dilute solution is highly advantageous, since it allows more complete surface coverage. Administration in two doses, as described above, is important, for coughing renders the first injection ineffective distal to the carina; however, the second injection gravitates to a lower level because of the prior anesthesia.

It will be noted that both injections are administered with the patient in the dorsal decubitus position. This position renders impossible an accident inherent in the intratracheal instillation of drugs in the upright or sitting position. When a drug is injected into the trachea with the patient sitting upright, regardless of the method, there is always the danger that the patient's position and particular anatomic configuration of the right lower bronchial tree will allow the direct gravitation of the drug to the dependent alveoli. The toxic manifestations of such an accident are similar to the intravenous injection of the drug. The administration of the anesthetic agent by the direct needle injection into

the trachea with the patient supine obviates this danger.

A few simple comments about the equipment may be helpful. In Figure 1, two 18-gauge needles may be noted next to the saline medicine glass. The first needle is used for aspiration of 3 cc. of 1 per cent pontocaine solution from the ampoules, its subsequent dilution and the first tracheal injection. After withdrawal from the trachea, this needle is discarded as contaminated, and the second needle is used for the second injection. When sterile pontocaine has not been obtainable, we have used 1.5 cc. of the conventional pontocaine 2 per cent topical solution, diluted, of course, to 9 cc. This necessitates the inclusion of a third needle for aspiration and dilution of the unsterile solution. Otherwise, the routine is similar; however, if one is to use an unsterile solution, great care must be exercised to avoid leak or injection of this solution in the needle tract between the skin and tracheal lumen.

Though there are theoretical complications, discussed below, the actual complications in the course of more than 1000 cases of tracheal anesthesia have been limited to 3 patients, who had superficial cellulitis of the soft tissues about the site of injection. One resolved spontaneously, and the others required 1-cm. skin incisions for drainage. These minor complications occurred more than five years ago, before adequate attention was given to pressure on the injection site and to the prevention of subcutaneous emphysema produced by air leak through the needle tract on coughing.

There are, of course, a number of possible dangers inherent in the technic described above. Often, our colleagues have asked about the dangers of infection spreading in the fascial planes. This has not occurred, and experience seems to justify our lack of concern over this complication. Another conceivable complication — namely, that of injecting the solution under the tracheal mucosa — does give us some concern. This might produce obstruction to the airway and must be carefully avoided by verification of the position of the point of the needle, by the aspiration of air before injection and by the immediate removal of the needle after the solution has been quickly injected. There have been no tuberculous sinuses even though the method has been extensively used in open cases of tuberculosis. However, we should not elect to use this method in the presence of extensive tuberculous disease of the larynx and upper trachea. There has been no bleeding from an aberrant thyroid isthmus.

Finally, the applications or limitations of this form of anesthesia in bronchoscopy for foreign-body removal are contingent upon the position of the foreign body itself.

Summary

A method of administering a dilute pontocaine solution for bronchoscopic anesthesia via the cricothyroid membrane directly into the trachea through a needle is described.

Technical details and the rationale of the maneuvers are outlined.

Theoretical and actual dangers are given consideration. The safety of the method is supported by experience in more than 1000 patients.

The value to patient and physician of a safe anesthetic technic that minimizes the discomfort of bronchoscopy is stressed.

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COEXISTING TUBERCULOUS AND MENINGOCOCCAL MENINGITIS*

Report of a Case

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MENINGITIS due to a simultaneous mixed infection is relatively rare. Neal[1] reviewed 3178 cases of meningitis and found that 26, or 0.8 per cent, were due to mixed infections. Unfortunately she did not break down these 26 cases into the different bacterial combinations that were present. Tripoli[2] studied 468 cases of bacterial meningitis and found 2 cases of mixed infection, an incidence of approximately 0.4 per cent. In a more recent study Hertzog[3] reviewed 377 cases of fatal meningitis with special reference to the bacterial diagnoses and collected 5 cases of mixed infection, or an incidence of 1.3 per cent.

Cases of tuberculous meningitis combined with a suppurative acute bacterial meningitis are even more unusual. Lemieux et al.,[4] in a review of the literature between 1900 and 1944, found only 20 reported cases of an associated meningococcal tuberculous meningeal infection. In the present review, an additional number of mixed cases of tuberculous meningococcal meningitis were discovered in the literature that had apparently not been found by those authors. Pipirs,[5] cited by Key,[6] studied 46 cases of mixed meningeal infection reported between 1896 and 1927 and found that the tubercle bacillus predominated as the primary organism. Cunningham[7] quotes Chalier and Guichard[8] as reporting in 1931 about 50 cases of combined tuberculous and meningococcal meningitis.

Regardless of the exact number of cases of combined tuberculous and suppurative infections of the meninges that have been reported, it was thought that the combination was unusual enough to justify presentation of the following case of a combined tuberculous and meningococcal meningitis.

CASE REPORT

A 26-year-old man was admitted to the medical service on January 30, 1945, with the diagnosis of nasopharyngitis. About 4 days previously the patient had mentioned to a friend that he was suffering from a severe headache. At sick call on the following day he was seen by a medical officer, who believed that he had an upper respiratory infection, prescribed aspirin and returned him to duty. On January 28, the patient had again gone to sick call because of persistent headache and because he felt too sick to do duty. He was afebrile. The medical officer again believed that this soldier was suffering from nasopharyngitis and recommended symptomatic therapy. On the following day, however, the patient was admitted to the hospital complaining bitterly of a severe headache, which seemed to be localized to the base of the skull. He was rational, but was so acutely ill that a thorough history was not attempted. He admitted vomiting twice.

Physical examination revealed a well developed, well nourished man who was co-operative and rational. There was marked rigidity of the neck; the patient complained bitterly when his head was flexed upon his neck. Neurologic examination revealed positive Kernig and Brudzinski signs, with a bilateral negative Babinski reflex. The remainder of the physical examination was negative.

The temperature was 98.8°F., the pulse 80, and the respirations 18.

A lumbar puncture was immediately performed, and several cubic centimeters of slightly cloudy fluid were removed for examination. A manometer was not available at the time for accurate determination of the spinal-fluid pressure, but it appeared abnormally high. Examination of the fluid revealed 774 white cells per cubic millimeter, with 54 per cent neutrophils and 46 per cent lymphocytes. The total protein was 270 mg. per 100 cc. Sugar was not found in the sample. A diagnostic stain of the spinal fluid was made, and two gram-negative diplococcic organisms suggestive of Neisseria were seen. Spinal-fluid culture was carried out, and at the end of 24 hours a luxurious growth of *Neisseria intracellularis* was present. A malarial smear was taken, since the patient had seen service in Sicily and Italy, but was negative.

The patient was immediately started on a therapeutic course of sodium sulfadiazine intravenously and fluids parenterally. During the day he was rational but complained of nausea and had frequent episodes of projectile vomiting.

On the morning of the following day the temperature was 101.6°F., the respirations 16, and the pulse 54. On that afternoon, intravenous administration of sulfadiazine was discontinued, and he was put on a dosage schedule of 1 gm. of sulfadiazine orally accompanied by 2 gm. of sodium bicarbonate every 4 hours. At 8:00 p.m. the temperature was still 101.6°F., and 20,000 units of penicillin intramuscularly was ordered every 3 hours. During the day the patient appeared rather irritable and mentally hazy and continued to complain of a stiff neck.

On the morning of the following day the temperature was 99.6°F., but by noon it had climbed to 101.2°F. A lumbar puncture was done and several cubic centimeters of cloudy fluid under elevated pressure were removed. Examination of the fluid disclosed 441 white cells per cubic millimeter, but no differential count was obtained. A smear for organisms was negative, as was a culture at the end of 24 hours. The temperature dropped to 99°F. by evening, but again climbed and at 3:00 a.m. on February 3 was 102°F. During the night he was incoherent and experienced a severe chill.

During the entire next day, the patient was mentally confused. He developed increasingly pronounced signs of meningeal irritation and during the morning had a severe clonic convulsion involving the right side of his body. During this attack, his pupils failed to react to light or accommodation and his left eye rotated inward. His temperature continued to climb and by midnight had reached 103.6°F.

On February 4 he continued to be restless and incoherent and had to be catheterized every 8 hours. Intravenous administration of fluids was maintained throughout the day.

On the following day the patient appeared much worse, developed Cheyne-Stokes respirations and was comatose throughout the morning. Doses of aminophylline and caffeine sodium benzoate relieved his respirations considerably. A lumbar puncture was done, and several cubic centimeters of opalescent fluid were removed. Examination of the fluid revealed 441 white cells per cubic millimeter, with 4 per cent neutrophils and 96 per cent lymphocytes. The sugar was 13.6 mg. per 100 cc., and the chloride 473 mg. per 100 cc. After the fluid had stood for 10 minutes, a delicate fibrin pellicle formed, but search of a stained smear revealed no acid-fast organisms, and a 24-hour culture for pathogens was negative. At the time this lumbar puncture was done, 10,000 units of penicillin was injected intrathecally, but after a report of the spinal fluid was obtained, it was considered useless to continue intrathecal medication on subsequent taps, and penicillin was discontinued. An x-ray film of the chest taken at the bedside showed some generalized increase in density of the left lower lobe.

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During February 6 the patient's condition remained about the same. He showed occasional moments of rationality but by afternoon had lapsed into complete stupor. Neurologic survey revealed loss of deep and superficial reflexes bilaterally with a positive bilateral Babinski sign. The Kernig and Brudzinski signs continued to be present. The pupils failed to react to light or accommodation, and the left eye continued to rotate inward. During the day he received fluids, sulfadiazine, oxygen and caffeine sodium benzoate intravenously. Examination of the blood showed a red-cell count of 4,410,000 and a white-cell count of 13,000, with 78 per cent neutrophils, 12 per cent lymphocytes and 5 per cent monocytes.

During the following day the patient remained comatose. Because of the high, fluctuating temperature a malaria smear was done and was found to be positive for *Plasmodium vivax*. A lumbar puncture during the day revealed 230 white cells per cubic millimeter, with 99 per cent lymphocytes. A very definite, fine fibrin pellicle formed within an hour of standing. Since quinine or atabrine for intravenous or intramuscular use was not available at that time, the patient was given 0.4 gm. of atabrine that evening by rectum. On the next day quinine dihydrochloride was obtained, and large doses were given intravenously and intramuscularly every 6 hours. By 6:30 p.m. on February 9 the patient's condition became terminal, and his temperature continued to rise during the night, reaching 107.4°F. by 4:00 a.m. At 6:00 a.m. on February 10 he ceased to breathe.

At autopsy the body was that of a fairly well developed man, revealing marked rigor mortis. The pupils were round and slightly unequal. When the pleural cavity was entered the lungs receded, and no excess pleural fluid was observed. The lungs showed no pertinent disease on either gross or microscopical examination, and no tuberculosis was found. Examination of the spleen was essentially negative, and despite multiple sectioning, no lesions were noted. Examination of the liver was also negative.

On examination of the brain the external appearance of the dura showed no abnormalities. It was incised and reflected, revealing a very markedly congested vessel over both cerebral hemispheres. In addition, there was a small amount of yellow material about the blood vessels, and occasional small white foci, approximately 1 mm. in diameter, were seen in the pia arachnoid. The brain was marked in the usual manner. It was of the usual size and shape, but slightly decreased in weight, which was 1280 gm. Over the base of the brain, there was a gelatinous, cloudy exudate, which was very abundant and which became yellow, opaque and purulent about the optic chiasm. This exudative process also clouded the leptomeninges covering the cerebellum. The multiple white, minute foci noted over the cerebral hemispheres were very numerous about the base of the brain and over the cerebellum. When the leptomeninges were dissected free, it was noted that they seemed to be contained within the meninges. Multiple coronal sections throughout the brain revealed some dilatation of the lateral and third ventricles. There was also a slight thinning of the cerebral cortex; however, there was no evidence of molding of the cerebellum about the brain stem. The superior portion of the caudate nucleus on the left contained red, softened areas measuring 0.8 cm. in diameter. The superior portion of the temporal lobe on the right contained a very soft area immediately adjacent to the sylvian fissue. The meninges were thickened in this area, and the superior portion of the temporal lobe was adherent to the undersurface of the parietal lobe. There was no yellow discoloration about the border of the region, and no evidence of hemorrhage into it. The tissue in this region was white, soft and friable, and no sharp line of demarcation delimited this area from the surrounding brain tissue. In a number of areas throughout the brain, small congested vessels were visible, and petechiae were suggested. There was no evidence of gross hemorrhage or necrosis in the thalamus or brain stem.

On microscopical examination of the brain many of the blood vessels of the leptomeninges were surrounded by a cuff of chronic inflammatory cells, chiefly lymphocytes and mononuclear cells. There was a fairly diffuse infiltration of the leptomeninges by chronic inflammatory cells. In some areas, often perivascularly, there were foci of cascous necrosis. Tubercle-like lesions were noted with large numbers of epithelioid cells and scattered, multinucleated Langhans's giant cells. Acid-fast stains of these areas revealed scattered acid-fast bacilli identical morphologically with tubercle bacilli. The chronic inflammatory infiltrate was also noted about the vessels in the Virchow-Robin spaces and in some areas deep within the brain substance. There was a fairly generalized congestion of the blood vessels of the brain, and in some areas, perivascular extravasation of red cells was present. The pineal body was surrounded by a similar inflammatory process. In a rare area, the peripheral substance of the brain was involved in a caseous necrosis for a short distance beneath the pia mater. However, the appearance was that of an extension of the meningeal process into the brain rather than vice versa. No true tuberculoma was noted. The softened area described grossly in the temporal lobe microscopically was composed of brain containing foci of hemorrhage and fragmentation of the brain substance with a few scattered polymorphonuclear leukocytes. The choroid plexus contained numerous small, round, calcific bodies, and a few of the vessels were surrounded by a cuff of lymphocytes. However, no marked inflammatory involvement or caseous necrosis was noted similar to that seen in the meninges. Occasional ganglion cells showed evidence of mild degenerative changes, with swelling and rounding of the cytoplasmic borders. There was a congestion and generalized slight increase in the glial cells throughout the brain.

Culture of the heart's blood revealed no growth.

A gram stain of the right lower lobe of the lung disclosed no organisms. On culture a nonhemolytic *Staphylococcus aureus* and a *Streptococcus viridans* were observed.

No malaria parasites were seen on a smear of the spleen.

A smear of the brain abscess demonstrated no organisms. Culture showed an alkaligenes bacillus; gram-positive cocci in chains and groups were overgrown by the gram-negative bacilli. On guinea-pig inoculation acid-fast bacilli were recovered from an inguinal lymph node and spleen.

On March 20 an autopsy of a guinea pig inoculated 38 days previously was positive for lesions typical of tuberculosis. Smears from the lesions showed the presence of acid-fast bacilli.

Discussion

This case was of unusual interest. What at the onset appeared to be an uncomplicated case of meningococcal meningitis terminated fatally with a tuberculous infection of the meninges and was further complicated by the recrudescence of a malarial infection that the patient had undoubtedly contracted during his service in Sicily and Italy. Because of the comparative rarity of a combined tuberculous and suppurative meningeal infection, it was thought of interest to review the literature. The cases reported in the medical literature since 1911 are presented in Table 1.

A review of this table shows that most of these case reports are from the foreign literature. The case presented above is the first reported from American sources, and is approximately the thirty-fourth case of its type in the literature. Since meningococcal meningitis has been found in many series to be the most common bacterial type of meningitis, it is not surprising that cases of tuberculous meningococcal meningitis predominate.

The record in this case reveals considerable similarity with those in the other reported cases. The patient entered the hospital with the classic signs and symptoms of meningitis. Although, unfortunately, there is no record of any bacterial cultures taken from the nasopharynx, it can probably be assumed that this was the initial focus from which dissemination to the meninges occurred. The

spinal-fluid findings were certainly compatible with a meningococcal meningitis, and it is possible that at the time of onset the patient had a pure meningococcal infection. In retrospect however, there is one finding that might be significant in view of the patient's subsequent course. This is the fact that despite the acuteness of the infection, only 54 per cent of the white cells were neutrophils. This is almost the same ratio of lymphocytes to neutrophils as was found by Fiddes[24] in a case of mixed tuberculous meningococcal meningitis in a fourteen-month-old baby. That this relative lymphocytosis in the face of a suppurative meningeal infection may be of significance is further strengthened by the findings of Claude et al.[15] These authors reviewed the literature and stated that in most cases an acute polymorphonuclear response in the spinal fluid is replaced by a lymphocytosis. Moritz,[21] in the report of a case of mixed tuberculous and Friedländer meningitis, also points out that the duality of the infection may alter the spinal-fluid findings. However, without some clinical findings to support the diagnosis of a tuberculous meningitis, it would be misleading in many cases to place too much emphasis on these findings alone.

After the institution of sulfadiazine therapy supplemented later by penicillin, the patient failed to respond clinically but continued a downhill course, despite the fact that, after three days of sulfadiazine therapy, smear and culture of specimens of the spinal fluid were negative for the meningococcus. It was not until after the patient had shown progressive mental deterioration and central-nervous-system damage that another lumbar puncture revealed the pathognomonic fibrin pellicle and the characteristic cell count and chemical findings of a tuberculous meningitis.

As in the majority of other reported cases of combined tuberculous and suppurative meningitis, the failure of the patient to respond to specific therapy was the clue that led to the suspicion that perhaps this was a double infection. Certainly, with no obvious manifestations of an active tuberculous process elsewhere in the body, there was no reason to suspect a tuberculous infection earlier. Many of the available case reports emphasize the fact that the diagnosis of a mixed infection can only be made bacteriologically and that the suppurative phase does not alter the progressive characteristic course of the tuberculous infection or establish any marked deviation from the usual clinical pattern. Since there is apparently no characteristic clinical picture of the mixed type of infection, it is possible that a certain number of such cases are missed, owing to the fact that complete bacteriologic studies are not always carried out because the possibility of a combined infection is not considered.

The central-nervous-system pathological findings in this case were characteristic of a pure tuberculous meningitis. In almost all the other reported cases in which chronologically the tuberculous phase appears to have been superimposed upon the suppurative phase, the pathological findings have been those of a tuberculous infection alone. These findings certainly suggest that the tuberculous invasion is secondary to the suppurative phase, although Moritz[21] believes that the pathological findings of the two types of meningitis are not sufficiently distinct to enable any conclusions to be drawn regarding the primary infection. That the pathological changes secondary to the acute suppurative phase may be masked by the changes resulting from the tuberculous infection is suggested in the findings of a case of mixed tuberculous pneumococcal meningitis reported by Achard and Horowitz.[22] At post-mortem examination of the brain, a typical basal meningitis most marked in the region of the fourth ventricle was present. The arachnoid was thickened, opaque and milky in appearance; areas of caseation were present in the floor of the fourth ventricle, and no findings characteristic of a suppurative meningitis were observed. However, both pneumococci and tubercle bacilli were cultured from spinal fluid taken from the fourth ventricle, and both organisms were found by smear and culture in adjacent areas of

TABLE 1. *Cases of Combined Tuberculous and Suppurative Meningeal Infection Reported in the Literature.*

No. of Cases	Bacteriologic Findings	Author
1	Tubercle bacillus and meningococcus	Guinon and Grenet[9]
1	Tubercle bacillus and meningococcus	Dupérié[10]
2	Tubercle bacillus and meningococcus	Bériel and Durand[11]
1	Tubercle bacillus and meningococcus	Gaudu cheau[12]
1	Tubercle bacillus and meningococcus	Loubet et al.[13]
2	Tubercle bacillus and meningococcus	Sainton and Maille[14]
1	Tubercle bacillus and meningococcus	Claude et al.[15]
1	Tubercle bacillus and pneumococcus	Devic et al.[16]
2	Tubercle bacillus and (?)	Vialard[17]
1	Tubercle bacillus and meningococcus	Achard et al.[18]
2	Tubercle bacillus and (?)	Colombe and Foulkes[19]
1	Tubercle bacillus and tetragenous organism	Todesco[20]
1	Tubercle bacillus and meningococcus	Aguirre and Bettinotti[20]
1	Tubercle bacillus and pneumococcus	Achard and Horowitz[22]
1	Tubercle bacillus and meningococcus	Imbert[23]
1	Tubercle bacillus and meningococcus	Mikulowski[24]
1	Tubercle bacillus and pneumococcus	Achard[25]
1	Tubercle bacillus and pneumococcus	von Cöke[26]
1	Tubercle bacillus and meningococcus	Schuman[27]
1	Tubercle bacillus and meningococcus	Grysez et al.[28]
1	Tubercle bacillus and meningococcus	Carloni[29]
1	Tubercle bacillus and meningococcus	Fox[30]
1	Tubercle bacillus and Friedländer bacillus	Moritz[21]
1	Tubercle bacillus and Friedländer bacillus	Moritz[21]
1	Tubercle bacillus and meningococcus	Cislaghi[31]
1	Tubercle bacillus and meningococcus	Fiddes[24]
1	Tubercle bacillus and meningococcus	Baur[32]
1	Tubercle bacillus and meningococcus	Todesco[20]
1	Tubercle bacillus and meningococcus	Lemieux et al.[4]

caseation. The case reported by Fiddes[34] is interesting in that two distinct types of exudate were present:

> On the ventral surface of the cerebellum and stretching forward to the pons was a thick greenish-yellow purulent exudate. Covering the midbrain and crura cerebri and running into the cerebral sulci along the vessels was a much thinner, whitish exudate, containing many miliary tubercles especially about the vessels of the Sylvian fissure. There was a great excess of spinal fluid in the ventricles. The brain was fixed and when examined later, both lateral ventricles were greatly dilated and many miliary tuberculomata were seen in their walls . . . .

The two different types of exudate described certainly suggest the combined effects of a suppurative and nonsuppurative type of pathologic process. In the findings in the case presented above, however, there was nothing to suggest the presence of a suppurative process, and to quote from the comments made by Colonel Harold L. Stewart, the pathologist, "the histologic findings and demonstration of acid-fast organisms leave little doubt regarding the type of meningitis, at least in the terminal phase."

The pathogenetic problems presented by this case are extremely interesting. Until the publication of the paper by Rich and McCordock[37] from Johns Hopkins in 1933, tuberculous meningitis was generally considered to be the result of hematogenous dissemination of the tubercle bacilli to the meninges. The reason for this was the high incidence of tuberculous meningitis found in association with cases of disseminated hematogenous tuberculosis. Rich and McCordock, however, believed that several factors lent doubt to the hematogenous theory explaining the pathogenesis of tuberculosis of the meninges. Because of these objections, they considered the rupture of a caseous tuberculous focus into the subarachnoid space to be a better explanation of the pathogenesis of tuberculous meningitis. This caseous focus might be in the adjacent vertebra, in the meninges themselves or in the brain or spinal cord. By very meticulous sectioning of the brains and spinal cords of 82 cases of tuberculous meningitis, the authors were able to demonstrate caseous foci in 77 cases, and in the 5 cases in which foci were not demonstrated, the examinations were not complete. This work of Rich and McCordock has been repeated and confirmed by other workers. MacGregor and Green,[38] for example, in examining 88 brains and spinal cords from cases of tuberculous meningitis, found caseous foci in 74 brains and evidence of tuberculosis of the spine in 4 other cases, making a total of 78 cases, or 88.6 per cent. In 59 of these cases, or 67 per cent, it was proved conclusively that the origin of the meningitis was from these caseous foci, and in a further 6 cases it was found highly probable, making a total of 74 per cent. In only 4 cases in this series were caseous choroid tubercles present, and the authors regarded these choroid-plexus foci as part of the diffuse meningitis and of no pathogenetic significance.

Although the work of MacGregor and Green tends to support the conclusions reached by Rich and McCordock, their findings have not always been substantiated. Ragins,[39] for example, studied 39 cases of tuberculous meningitis and found that in 32 cases (82 per cent) the meningitis resulted from direct hematogenous spread from some focus of visceral tuberculosis found at autopsy. In another series of cases, Engel[40] studied 15 cases of tuberculous meningitis superimposed upon generalized miliary tuberculosis and failed to discover in a single case caseous foci that could be considered the source of the meningeal infection. In all cases the choroid plexi were involved microscopically with an acute tuberculous process with tubercle bacilli present in every case. The author reached the conclusion that infection from the choroid plexus was a more important factor in the pathogenesis than the rupture of a caseous focus into the subarachnoid space.

In the case reported above, the source of the tuberculous meningitis remains a mystery. No visceral focus of tuberculosis was found in any of the organs examined. It was suggested by Colonel Stewart that perhaps some small tuberculoma had been overlooked in the sections of the brain examined. and this remains the best possibility. Both Rich and McCordock and MacGregor and Green mention the ease with which a small tuberculoma may be overlooked unless particular care is taken during the sectioning. The former group emphasize the fact that the brain sections should not be more than 3 mm. in thickness and that special technics must be employed in many cases to demonstrate tuberculomas that are fresh and not yet encapsulated. In this case no mention was made of the number or thickness of the sections examined or the technic employed.

There were several other possible sites in this case for caseous foci that might have ruptured into the subarachnoid space, but in none of them is the possibility anything but remote. There was no evidence of any active caseous foci in the choroid plexi. It has been mentioned that a vertebral lesion may be the source of a tuberculous meningitis, and in this particular case there is no mention that this possibility was completely excluded by x-ray or pathological examination. However, it is unlikely that such a focus existed since the patient had no complaints suggestive of a vertebral lesion. Crowe[41] has demonstrated that a tuberculous otitis media can be the source of direct meningeal invasion in tuberculous meningitis, but this patient had no complaints referable to his ears and examination of the ear, nose and throat upon admission had been negative. There is one other possibility that was not wholly precluded since a complete examination of the spinal cord was not

performed: a spinal-cord tuberculoma that had ruptured into the subarachnoid space, causing a meningitis.

Single or multiple tuberculomas of the spinal cord are not common. By 1943 only 93 cases had been reported in the literature.[42] The most comprehensive review of the subject of spinal-cord tuberculomas was published by Thalhimer and Hassin[43] in 1922. These authors collected 67 cases and reported abstracts on 58. As might have been expected, almost every case presented symptoms suggestive of an expanding spinal-cord lesion that, in the majority of cases, was diagnosed clinically as a spinal-cord tumor. The cases of spinal-cord tuberculoma examined at autopsy often revealed microscopical and gross evidence of a localized tuberculous meningitis about the nerve roots, with extension of the caseous process up to and sometimes into the subarachnoid space. In the case reported above, however, because of the lack of any symptoms referable to the spine and especially because of the failure to find any active tuberculous focus elsewhere that could have acted as a feeding lesion, a spinal-cord tuberculoma producing meningitis is unlikely.

The relation between the suppurative and the tuberculous phases of this patient's illness is an interesting one. Certain writers, such as Claude and his co-workers,[15] considered the association coincidental. Moritz[21] believed that the tuberculous infection was primary, even though the tubercle bacillus did not appear in the spinal fluid until the day before death and although the Friedländer bacillus was found after the first lumbar puncture. Lemieux et al.[4] also regarded the suppurative phase of the dual infection as secondary.

Other authors, however, have thought differently. In a case of mixed meningococcal and tuberculous meningitis reported by Schuman[27] in a six-year-old boy who, three weeks before the onset of meningitis, had had an attack of measles, it was believed that the measles had activated a dormant tuberculous lesion of the lung, with a resultant meningitis. In another case of a combined tuberculous meningococcal meningitis reported by Grysez and his associates,[28] the meningococcal infection was considered to have activated a latent tuberculous focus. From the clinical and pathological evidence in this case, this mechanism seems the most likely explanation.

Baum and Amberson,[44] in a study of cases of pulmonary tuberculosis existing concomitantly with bronchiectasis, lung abscess and pneumonia, have demonstrated conclusively that a latent focus can be activated by a suppurative process: "Suppurative disease has been found repeatedly to be responsible for the activation of a tuberculous process, the mechanism most likely being destruction of the capsule with consequent liberation of the tubercle bacillus." If such a mechanism can be held responsible for the activation of a pulmonary focus, the same mechanism can be held responsible for the activation of a subarachnoid focus, too small to have been demonstrated on sections. The problem of the exacerbation of the old malarial infection is perhaps even more obscure than the problems of pathogenesis raised by the dual meningeal infection.

Summary

An additional case of coexisting tuberculous and meningococcal meningitis is reported, and the pertinent literature is reviewed.

The pathogenesis of the inter-relation between tuberculous and suppurative meningitis is discussed.

It is hoped that further cases will be reported as they appear.

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PROPHYLAXIS AGAINST ALLERGY

A Pediatric Program

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THE pediatrician holds a unique position in the field of allergy. To him falls the opportunity of dealing with the patient before the first manifestations of allergy. Therefore, whatever can be achieved in the way of preventive allergy lies within his sphere.

Allergy is defined as an altered reactivity of tissues following the introduction of foreign protein by inhalation, injection or ingestion. The difficulties of taking prophylactic measures in the field of allergy are inherent in its definition. In general, it is only after the occurrence of clinical symptoms that steps are taken to eliminate the offending allergens when possible, or to protect the patient by hyposensitization when indicated. Logically, many symptoms might be avoided by elimination or by guarded exposure prior to sensitization. Present knowledge is such that much foresight can be exercised.

In the evolution of the literature dealing with allergy, many equivocal and some contradictory findings appear. Many data, however, have been well established. Together with advances in clinical experience, this knowledge provides at least the foundation of a plan for prophylaxis.

The inheritance of the tendency to develop allergy is now generally accepted. Repeated observations of most clinicians, regardless of the variation in their figures, force the conclusion that the children of allergic adults will constitute the greatest number of allergic persons in the next generation. It is the purpose of this paper to outline a regime for this group of potentially allergic children by which the danger of sensitization to certain potent allergens may be minimized.

HEREDITY OF ALLERGY

Vaughan[1] has summarized and evaluated the numerous statistical studies concerning the heredity of allergy. His figures indicate that about 10 per cent of the general population suffer from major allergy and that another 50 per cent have minor allergy. There is an antecedent family history of allergy in from 50 to 70 per cent of allergic patients whereas only 7 per cent of nonallergic people give a family history of allergy. Differences in methods of statistical classification employed by the various writers apparently account for the variation in their figures.

Table 1 illustrates this variation.

Vaughan concludes that there is a hereditary factor in allergy. He estimates that about 75 per cent of all children with bilateral allergic inheritance and about 50 per cent of those with unilateral inheritance will eventually develop some type of allergic manifestation. The heavier the inheritance, the greater the number of allergic symptoms and the earlier they will appear in each offspring.

TABLE 1. *Types of Allergy in Relation to Positive Family History.**

ALLERGIC MANIFESTATION	POSITIVE FAMILY HISTORY
	%
Asthma (in children)	40-70
Asthma (in adults)	40-60
Migraine	75-85
Food allergy	68
Eczema	28-76
Urticaria	25-55

*Adapted from Vaughan.[1]

Since the earliest indication of this potentiality lies in the parental history, the importance of determining the presence or absence of allergy in the parents of the newborn by carefully taken case histories becomes evident. The program for the care and feeding of such infants during their first year of life can be guided by such information. Although all children of allergic parents need not become allergic themselves, their potentialities must certainly be reckoned with as a group.

Mechanism of Sensitization

The mechanism of sensitization depends on the type of allergy involved. The inhalants, as the name suggests, occur in the environment of the patient or in the atmosphere, creating sensitization through the respiratory tract. Pollens, ubiquitous and probably uncontrollable, fall into this category. Other inhalants, such as feathers and animal dander, are controllable. Allergens found in food cause symptoms upon ingestion, and these symptoms are alleviated by diet.

The presence of the allergic tendency, whether inherited or acquired, does not result in clinical allergy unless sensitization occurs by exposure to potent allergens. A large part of allergic treatment consists of elimination of offending allergens from the environment or the diet. This clinical procedure has given excellent results. Is it not wiser, then, to avoid exposure, thereby substituting prevention for the need of a cure?

The factor of food allergens is most important at the earliest period of life. Fortunately for this group, the dietary intake is most readily regulated at this time. Adequate infant feeding has two major requirements: normal growth must be maintained, and minimum vitamin and mineral requirements must be fulfilled. These two basic requirements can be met, while, at the same time, the exposure to potent allergens is lessened.

Food allergy has been recognized for many years, but it was not until 1916 that Schloss and Worthen[2] gave the first hint of its mechanics. In their classic paper they proved that foreign proteins are absorbed in unchanged form through the gastrointestinal tracts of normal infants and to a greater degree in those suffering from debility or any form of gastroenteritis. In 1920 Schloss[3] described the hyperacute type of sensitivity to food as evidenced by urticaria, asthma and symptoms of shock. The diagnosis of this condition is commonly made by the parents because of its obvious cause and effect relation. The symptoms are so distressing that the detection of the offending food is never a problem. Another type of sensitivity that brought on gastrointestinal disturbances with vomiting and diarrhea or skin manifestations such as eczema was described by the same author. In 1925 DuBois, Schloss and Anderson[4] reported that enteral absorption of antigenic protein by normal or marasmic infants led not only to the appearance of a specific precipitin in the blood but also, in many cases, to cutaneous sensitivity. This fundamental work has been repeated by Wilson and Walzer[5] and other investigators.

Schloss and his co-workers[6] stated that the mechanism whereby the body is protected from the continued absorption of appreciable amounts of foreign protein was unknown. This statement still holds true today. They advanced three possible explanations, which continue to be of great interest: by some means the gastrointestinal wall becomes impermeable to each newly introduced protein after it has been ingested for a certain length of time; an alteration in the digestive enzymes takes place so that they ultimately become capable of producing complete denaturization; and finally, even though foreign protein is absorbed as such, it may be neutralized by some hitherto unrecognized immune reactions. It has been observed by Rackemann[7] and others[8] that children frequently manifest the first symptoms of hypersensitivity to antigenic substances a few days or weeks after initial exposure. This interval coincides with the development of the antibodies as observed by Schloss and his co-workers.[6] In the average infant this immunologic process is passed over without incident. In the infant with the inherited tendency to hypersensitivity, Schloss and his associates[6] have reasoned that this mechanism may be altered so that the clinical manifestations of allergy result.

Basic Foods in Infant Feeding

The basic foods in infant feeding are milk, egg, wheat, orange juice and fish oil. These foods are added to the diet at varying ages, depending on the fashion of the moment and, to a lesser degree, on the school of thought to which the practicing pediatrician subscribes. Allergists[9] have found these five foods to be the most common sources of allergic manifestations in infants and young children. Laboratory workers have used the same allergens to prove the absorption of undigested protein through the gastrointestinal tract. Thus, there is the rare circumstance of five basic foods, ever-present in infant feeding, that are potent allergens and are readily absorbed unchanged through the mucous membrane of the gastrointestinal tract.

In summary, a large number of infants are potentially allergic by reason of heredity. Five basic food requirements of the infant diet are potent allergens, and these proteins are absorbed unchanged through the gastrointestinal tract. Is it not logical, then, to diminish the potency of these allergens by introducing them into the diet in a denatured form or to avoid them whenever possible?

Milk holds a unique position in the infant diet, unparalleled by any one food in adult life. Hill[10] pointed out that the infant takes enormous quantities of milk in proportion to his weight. He

asserted that nature never intended the infant diet to have so high a protein content as that furnished by cow's milk and that the infant's digestive function is not adapted to this milk.

There are two proteins present in milk: the more common offender, as Hill and Pratt[11] have pointed out, is lactalbumin; the second is casein. Anderson, Schloss and Stuart[12] demonstrated the close biologic relation between goat, cow and human casein. This explains why casein-sensitive patients do not benefit when the milk ingested is changed from one type to another. Lewis and Hayden,[13] in 1930, reported a diminution of antigenic properties in heated milk. Ratner[14] supported this view by pointing out the diminished antigenicity of evaporated cow's milk, owing to the prolonged heat applied in evaporation. Because of its method of manufacture, this does not hold true of powdered milk.

Egg allergy in infants and children is relatively common and important. As early as 1907, Gelbke[15] reported marked clinical response to the ingestion of egg. The cases reported were of the immediate, dramatic type, the symptoms developing instantaneously from the slightest contact with egg. This high degree of sensitivity does not represent the most frequent type of reaction. The slow, masked type of reaction is more common. In Vaughan's[1] experience, corroborated by Hill and others, egg appears to cause cutaneous manifestations more frequently than other symptoms.

There are a few cases on record in which egg sensitization appears to have been hereditary. This situation is evidenced by the occurrence of symptoms on the first exposure to this food. These cases are the exception rather than the rule.

Although egg white is the most frequent source of trouble, the egg yolk cannot be considered blameless. Egg white is the most difficult of all proteins to digest completely. Walzer[16] has found that incompletely digested egg protein circulates normally in the blood of some infants after feedings.

There are at least three aspects to the problem of egg as an allergen. Foremost is the prevailing custom of early introduction of egg into the diet of infants. Undigested egg protein circulating in the blood makes sensitization much easier in the potentially allergic infant. The second is the inability to denaturize egg by heat or any other known procedure. The third, and equally important, is the frequency with which egg is used in the preparation of other foods.

Wheat is also an ubiquitous allergen. Less potent than egg, it is also ingested in large quantities at an early age by most infants. Of 63 prepared cereals and infants' foods that contain wheat, 39 convey by their trade names no suggestion of the presence of wheat. Whether or not the allergenicity of wheat is diminished by heat in its preparation is still a disputed point. It is sufficient to say that the early ingestion of wheat together with the failure to recognize its presence in many prepared foods makes this allergen an active one in the infant. Rarely does wheat cause the type of acute syptmom complex associated with a potent allergen such as egg.

Fish as an allergen in infancy may seem paradoxical since fish is not often included in infant feeding. When, however, one considers that thirty species of fish are recognized and allowable as the source of *U.S.P.* cod-liver oil, its importance becomes evident.

Clinically, fish may cause either an acute or a delayed type of reaction. In the hypersensitive patient the odor of fish may cause asthma. Denaturization here is again difficult. Clinically complete avoidance has been the most expedient course. Since cod-liver oil, or at any rate, vitamins A and D are added to the infant diet at a very early age, care must be exercised in handling this potent allergen.

Another essential in all infant feeding is vitamin C. This is usually added to the diet at an early age in the form of orange juice. Sensitivity to orange juice does occur. Even the artificial coloring added to most oranges has been known to cause allergy. Denaturization by heat is impractical because it destroys the vitamin C content.

Prophylactic Treatment of the Potentially Allergic Infant

The prophylactic treatment of the potentially allergic infant must begin at birth. Every child in this category must be carefully watched for the first sign of an allergic manifestation. Before any symptoms develop, the following procedures are recommended to avoid, whenever possible, exposure to active allergens.

The period necessary for the development of symptoms after the introduction of a new food is not definitely known. The work of Schloss et al.,[4] Rackemann[7] and Hill,[10] in addition to personal experience, has prompted the adoption of an arbitrary time of fourteen to twenty-one days as a trial period. Immediate symptoms are detected readily, and such a trial period allows sufficient time for cumulative effect to become apparent.

When the trial period has been passed safely, a food may be considered nonallergenic for the patient under consideration. The next danger lies in the continual daily or even twice daily ingestion of the accepted food. This hazard may be overcome by rotation of diet. For example, if cereal is given daily, there should be a rotation of cereals: wheat one day, rice the next day and oats the following day. Vegetables and meat should also be rotated.

The pediatrician's first concern for any newborn infant is a formula on which the infant can thrive. Evaporated milk is the first choice whenever breast feeding is not feasible. The low antigenicity of the lactalbumin in evaporated milk has been firmly established. Care should be exercised to determine that cow's milk is not first given as a matter of hos-

pital routine. This may lead to sensitization later. If allergic symptoms do appear on an evaporated-milk formula, it is safe to assume that milk casein is the offender and no type of animal milk will improve the condition. In these cases, which fortunately are rare, soy-bean milk should be substituted. Once evaporated milk has been instituted and no symptoms occur, it should be continued as the only type of milk given for the entire first year of life. At the termination of this period, absorption of undigested protein through the intestinal tract is less likely to occur.

An essential ingredient in every infant's formula is the added carbohydrate. Corn syrup in the form of Karo is commonly used for this purpose. Randolph[17] suggests that corn in all forms is a potent allergen. More work may be necessary to confirm this finding, but its probable allergenicity can be avoided with ease. Dexin, a product of Burroughs and Wellcome, does not contain corn sugar but has been found excellent in infant feeding. Such a simple substitution is worthy of trial.

Between the ages of one and four weeks it is essential to add vitamins A, D and C to the average infant's diet. In the group of potentially allergic children, this should be done by the use of ascorbic acid for vitamin C and provatol or any other synthetic for vitamins A and D. By these simple expedients one can avoid exposure to fish oil or natural orange juice. Here, too, avoidance should be continued at least until the infant has reached one year of age.

The proper age for the introduction of solid foods into the infant diet has long been a disputed point. In view of the ease with which undigested protein is assimilated through the gastrointestinal tract of the infant, caution should be exercised. Three or four months of age seems a proper time, albeit an arbitrary one.

As important as the age of introduction of solid food is the type of food selected for each increase in the infant diet. Since the infants under discussion are readily sensitized by any type, it is imperative to introduce one simple food at a time. For some years it has been the custom to start with prepared cereals such as pablum and cerevim. Unfortunately these cereals represent combinations of cereals that are not indicated by their trade names. Should sensitization occur, identification of the offending allergen becomes very difficult. Pablum, for example, contains farina, oat meal, wheat germ, yellow corn meal, powdered beef bone, powdered alfalfa leaf and powdered yeast. Cerevim contains whole-wheat meal, oatmeal, wheat germ, powdered skimmed cow's milk, yellow corn meal, dried brewer's yeast, barley and malt.

I prefer the introduction of cereals in the form of rice, the least antigenic of all the cereals. Wheat may be introduced, but in a pure form, such as cream of wheat. Then, if allergic symptoms occur, identification of the offender is facilitated.

Egg may then be introduced as hard-boiled yolk. If no reaction takes place after two to four weeks of daily ingestion, one may safely assume that no sensitization has occurred, and proceed to add egg white in small quantities.

At about the age of six months, vegetables may be introduced. There is a growing tendency to use combinations of vegetables at the start. This procedure should be avoided. Single vegetables added at an interval of two to four weeks will simplify the identification of a sensitizing agent. After a sufficient number of vegetables have been tolerated, the infant is ready to be given vegetable soups, but in offering such mixtures, one must avoid the use of commercial soups that often contain "fillers" such as barley.

Beef juice may be introduced at about eight or nine months of age. If well tolerated in the allergic sense, one different well cooked meat may be added at each monthly change of diet.

Although in the potentially allergic infant, food is of prime importance in precipitating allergic manifestations, environmental factors cannot be exonerated. Fortunately, the environment of infants can be controlled. Care must be exercised from the moment the infant is brought home from the hospital, and precautionary measures must be taken in the establishment of allergic cleanliness in the nursery. The infant's mattress should be covered with a dust-proof covering. Better yet is the use of the newer foam-rubber mattress. Feather pillows should be avoided. The new glass-fiber pillow is a good substitute. No feather puffs or comforters should be permitted in the room. Wall-to-wall carpeting with ozite padding is inadvisable in the nursery. Linoleum, which can be kept free of dust, is ideal. Washable glass curtains can be substituted for heavy draperies.

No insect sprays or pyrethrum compounds should be used in the nursery. There is no point in exposing potentially allergic infants to heavy doses of pyrethrum, which is closely related to ragweed pollen.

No wooly stuffed toys should be introduced for these children to play with. These toys are commonly stuffed with cotton lint or kapok, both of which are potent allergens.

The hygiene of an infant requires the frequent use of baby powder. It is a simple matter to provide a nonallergic dusting powder. Highly scented baby oil should also be avoided. Shampoo lotions as allergens are well recognized, and such lotions need not be employed. A simple castile soap will serve adequately.

Domestic-animal contacts in the home are one of the commonest sources of early sensitivity. If the introduction of dogs, cats, birds or rabbits into the homes of such infants is avoided, a great deal of difficulty in later life may be averted.

The problem of pollen sensitivity, which is common in early life, may be raised at this point. The unequivocal answer to this question must be that nothing can be done to prevent such sensitization. It seems likely, however, that environmental or dietary factors are often operative first in destroying the allergic balance of the potentially allergic infant.

Discussion

This article offers no statistics supporting its proposed program. Any valid statistical study would require large numbers of patients observed over many years. Since the study of inheritance is so complicated, reports of individual cases successfully avoiding allergic manifestations can neither refute nor support the aim of the proposed regime for allergic prophylaxis.

The maintenance of allergic balance is considered very important in the potentially allergic person. Often a minor sensitization is believed to set off an extensive chain of symptoms. In infancy every precaution that may defer the upset of this balance should be taken.

A program such as that set forth is readily carried out. It calls for no major deviation from generally accepted practice in infant care. All that is necessary is a knowledge of the infant's inherited allergic tendencies, together with an awareness of the relative allergic potencies of each of the major foods and inhalants.

If prophylaxis fails in this group, a new awareness of the sources and onset of allergy will make detection of offending substances much simpler.

Summary

An attempt is made to define the potentially allergic infant and to review the current information about the mechanisms involved in the development of allergy. In the practice of allergy, many cases are studied that require the removal of offending foods as well as other allergens. Their elimination is generally advised only after symptoms have developed. Clinical experience has shown the importance of five major food allergens. On the basis of the information provided by the literature and clinical knowledge, a program is outlined for the control of environment and of food intake that has as its aim the prevention of allergic symptoms in infants. This program is presented as an aid to those taking care of children and employs no radical deviation from the accepted procedures of pediatric care.

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AN UNUSUAL COMPLICATION OF MILLER-ABBOTT INTUBATION

Report of a Case

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INTUBATION of the small intestine has become an invaluable diagnostic and therapeutic measure, so fundamental that when indicated it is used routinely and not extraordinarily. Too often, however, a procedure seems to attract attention proportional only to its novelty. All are concerned with what an intestinal decompression tube is doing for the patient, but few are concerned with what is being done for the tube so long as it appears to be functioning.

There is much literature on intubation. It teaches that the procedure should be used with deliberation at all times. This report stresses care in its use routinely, especially when it is decided that the tube be removed: it is not intended fully to discuss the subject.

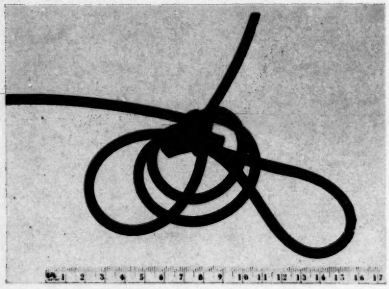

FIGURE 1. *Knotted Mass of Tubing Extracted from the Nasopharynx.*

Complications arising from ill advised use of intubation are obviously the most serious. In strangulation, for example, when the tube is considered more than an adjunct, disaster is inevitable. Here, intubation can serve only to mask the gravity of the situation.[1] Temporizing in cases of excellent functioning of the tube without clinical improvement of the patient is treating the tube and not the patient. Conversely, a tube that refuses to function in a patient who is definitely getting better carries no weight for intervention.[2] A further contraindication is the treatment of obstruction of the large intestine with distention of a segment of bowel defined by the point of obstruction and the ileocecal valve.[3] While generalized distention is abating a closed segment is maintained under localized distention because of the unilateral flow permitted by the valve.

The preparation of the tube for the patient is a primary consideration. It must be inspected carefully before it is passed. It must be clean, deodorized, without leaks and, above all, patent. The Miller–Abbott balloon should have sufficient slack to prevent curling of the tip after it is inflated.[1] Whenever mercury is used the operator must be certain that it will not escape. A report, including 2 cases of mercury free within the gastrointestinal tract, shows that mercury is not absorbed and, therefore, not toxic. It is unreasonable, however, to elaborate devices designed to aid in the passage of the tube and at the same time to permit the escape of their essential element.[4]

Several measures that are sometimes indicated better prepare the patient. Small doses of morphine and atropine about half an hour before intubation have two functions. Apprehension is often reduced to a desirable minimum. It has been suggested moreover that fear and excitement not only deprive the patient of co-operation but also tend to produce hypertonicity of gastric cardia and the pylorus, two most important obstacles a tube must overcome. For patients with small nasal passages and for those who are hypersensitive, a solution of ephedrine and pontocaine will provide extra room and will lessen sensation.[4] None but experienced personnel should attempt to pass a tube of any sort, or more precisely, no one who does not appreciate his limitations should be allowed to pass a tube. Recently a well meaning attendant decided to pass a tube that the patient had dislodged. She admitted that there was considerable coughing and gagging but could not believe that this caused the patient to lose his voice for two months. An ear, nose and throat specialist described the vocal cords as edematous without any other signs of trauma. It is quite conceivable that at the time it occurred the incident could have led to serious respiratory embarrassment.[5]

Once in the stomach the tube should be passed *pari passu* with its progress through the pylorus, never faster, for curled tubing in the stomach serves no purpose except that of creating the complication reported below. It is agreed that x-ray examination and fluoroscopy are the only infallible indicators of the position of the tube. The thick mucinous secretions of the stomach, which tend to bog the advance of the tube, can partially be neutralized by allowing clear fluids by mouth temporarily. Electrolytes thus washed away must be replaced quantitatively. The literature contains innumerable discussions of this relation.[6] Frequent irrigations of the tube are always indicated.

A most serious complication has been reported recently by Berger and Achs,[7] who describe a case

in which the tip of the tube actually perforated the small intestine. It appears that little can be done to prevent perforation except the discontinuance of the procedure as soon as possible.

When it is thought that the tube is no longer necessary it is good policy to stop suction a reasonable length of time before the actual withdrawal.[1] Leigh, Nelson and Swenson[2] believe that a tube should either reach a definite obstruction or proceed as far as the cecum in all cases before it is removed.

The following brief case report describes an unusual development encountered during the withdrawal of a Miller–Abbott tube.

Mrs. E. F. (B.I.H. 92980), a 72-year-old woman, was admitted to the hospital on February 28, 1947, after she had sustained an incomplete intertrochanteric fracture of the femur. Buck's extension apparatus was applied, and the patient did well until March 6, when she began to suffer from ileus. Nausea, vomiting and mild distention led to the use of a Miller–Abbott tube, which relieved her distress. On March 9 withdrawal of the tube was attempted, and during this maneuver the patient developed serious respiratory difficulty, and became moderately cyanotic. The tube seemed to be fixed when the markers indicated that about 120 cm. was still to be withdrawn. The pharynx was inspected, and three lengths of tubing could be seen lying against the posterior wall. One of the lengths was grasped and the knotted mass of tubing shown in Figure 1 was extracted from the nasopharynx.

Discussion

In this case the tube was used as a therapeutic measure primarily, intrinsic intestinal disease merely being kept in mind. There was no reason strongly to suspect either mechanical obstruction or physiologic obstruction other than on the basis of a benign ileus. Because there was clinical evidence that the tip was past the pylorus (almost pure bile in the drain bottle soon after it was passed) and because almost immediately the tube was successful in relieving the patient's distress, no x-ray examination was carried out. The tube was passed on the assumption that it was in the small intestine.

Only in retrospect is the value of knowing everything possible about the tube demonstrated. The knot should certainly have been discovered had routine x-ray or fluoroscopic study been carried out. Because this complication is preventable and can be circumvented by anticipation when discovered this case is reported. A similar incident could occur with any of the modifications of the original Miller–Abbott tube.

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PRIMARY ATTACK OF VIVAX MALARIA OCCURRING TWENTY-SEVEN MONTHS AFTER INFECTION*

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TROPICAL diseases, particularly malaria, have assumed greatly increased diagnostic and therapeutic importance in this country with the return of servicemen from endemic areas.[1–4] Studies of the natural course of relapsing vivax malaria[5, 6] have led to the prediction that cases of this disease, acquired in the Southwest Pacific, would continue to appear for at least three years after the return of the last serviceman.[4–7] In addition, the use of quinacrine (atabrine) for the suppression of malaria has delayed the onset of the primary attack for months, whereas the normal intrinsic incubation period is eight to seventeen days.[8] Discontinuance of suppressive therapy in infected subjects is usually followed by symptoms within two to ten weeks, but occasionally the first clinical symptoms of malaria may be delayed for months. Reviews of the Army and Navy experience have indicated that the longest interval thus far observed in such cases from last exposure to onset of the primary attack has been eighteen months.[7, 9]

This report records the occurrence of the first symptoms of vivax malaria in an ex-serviceman twenty-seven months after his return from an endemic area.

Case Report*

A 28-year-old married salesman entered the hospital on December 6, 1947, complaining of chills and fever. Five days prior to admission, he had awakened with a mild, generalized headache, stiffness in his neck muscles and slight malaise. The headache and malaise increased during the day, and by evening he felt alternately chilly and feverish. On the following morning he felt better, but his symptoms returned that afternoon and his temperature reached 102.2°F. Three days before entry, he was given penicillin orally because of persistent symptoms and a temperature of 103.1°F. On the next afternoon, his headache became severe, and he experienced a shaking chill of 2 hours' duration during which his temperature rose to 104.9°F., and he became delirious. Drenching sweats followed, and

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*This case is reported through the kindness of Dr. Harley A. Williams.

by the morning of the day prior to admission his temperature was normal and he was essentially asymptomatic. Another severe chill accompanied by prostration and delirium occurred the next day and he was hospitalized.

The past history included 2 years of military service, 1943–1945, in New Guinea and the Philippines. During this time the patient had had no illness requiring hospitalization and no symptoms suggestive of malaria. He took suppressive quinacrine daily until his return to the United States in September, 1945. He remained in Northern Ohio and had suffered only minor respiratory illnesses since that date.

Physical examination showed a well developed and well nourished, acutely ill man, who was rational, but weak and drowsy. Slight conjunctival injection and a firm, nontender spleen palpable 3 cm. below the costal margin were the only abnormal physical findings.

The temperature was 103.1°F. by rectum, the pulse 106, and the respirations 24. The blood pressure was 110/66.

Examination of the blood showed a red-cell count of 4,800,000, with a hemoglobin of 12 gm. per 100 cc., and a white-cell count of 8800, with a normal differential. Routine urinalyses showed no abnormalities. An aerobic blood culture was sterile. Cultures of the throat and sputum failed to detect pneumococci, beta-hemolytic streptococci or staphylococci. An anteroposterior roentgenogram of the chest was interpreted as showing accentuation of hilar markings but no definite infiltration. Examination of thin blood smears at the time of admission showed no malarial parasites. A thick film was not made until the next morning, when the temperature was normal. This and subsequent smears were negative.

Without therapy, the patient's temperature fell to normal within 12 hours and he remained afebrile and asymptomatic until discharge on the 5th hospital day. Despite the failure to demonstrate the parasites, his clinical picture was very suggestive of malaria. Moreover, it was learned that he had received 1.0 gm. (15 gr.) of quinine on the morning of admission. The diagnosis was confirmed when he was readmitted 6 days later because of recurrent chills and fever. His physical findings were unchanged, but many colonies of *Plasmodium vivax* were demonstrable in routine blood smears. Quinacrine therapy induced a prompt remission, and he was discharged free from symptoms.

Discussion

This case, with the long latent period, raises the question of a more recent exposure and illustrates the diagnostic difficulties that may be encountered in a patient with malaria. Since rare cases of malaria apparently acquired in the Cleveland area have been observed,[10] it is possible that this patient's infection was contracted locally. Against this possibility is the time of year, December, the known previous exposure in a highly endemic area and the size of the spleen. Such splenomegaly suggests, according to Boyd,[1] reactivation of a latent infection.

The onset of fever, which was at first sustained but later remittent in the tertian pattern, resembles that seen in the first attack of natural malaria[8] or that observed in many delayed primary attacks.[6–9]

Early administration of only a small amount of quinine was sufficient to halt the paroxysms temporarily, confuse the clinical picture and delay diagnosis. Use of a sulfonamide might have produced the same result.[11]

Although the usual incubation period of unmodified malaria is approximately eight to seventeen days, longer natural latent periods have frequently been observed. Shute[12] recently reviewed the problem of latency and long-term relapses in malaria and reported an average latent period of two hundred and eighty-two days in 9 cases under natural conditions. He pointed out cases, particularly those reported fro the Netherlands, of attacks in early spring from infection acquired the previous summer or autumn. Students of the disease are familiar with the occurrence of the first malarial attack upon arrival in a cooler climate, and protracted latent periods of ten months are mentioned.[13] No account was found of a *primary* attack occurring as long as twenty-seven months after the last exposure.

It seems reasonable to attribute this alteration in the incubation period of the disease to quinacrine. Wartime experience showed that the mechanism of quinacrine protection in vivax malaria is not destruction of the infective organism but reduction of parasitemia to a level insufficient for the production of clinical symptoms.[4] Delayed primary attacks indicate prolonged survival of the postulated fixed-tissue or exoerythrocytic stage of the parasite, or a degree of immunity that, until altered, is able to suppress the parasitemia to subclinical levels. The present concept that malarial immunity is dependent on the occurrence of frequent relapses[6] tends to eliminate this factor in the case reported above.

Baker and Platt[14] reported a study of troops heavily infected with malaria on Guadalcanal and subsequently maintained on quinacrine suppression for eighteen months after their transfer to nonmalarious areas. A greatly reduced relapse rate was noted during a three-month period of observation following withdrawal of quinacrine. Subject to the limitations of this period of observation, the authors concluded that "not only is the high malaria rate in heavily seeded troops temporarily controlled by atabrine suppressive medication but a highly significant amount of clinical vivax malaria is permanently abolished." It is difficult, as they suggest, to know whether to ascribe such apparent cures to the medication or merely to the passage of time with the development of immunity. The patient in the case reported above did not develop clinical malaria until more than four years after his first possible exposure and more than two years after his last exposure. Two years of suppressive quinacrine therapy during exposure did not prevent the eventual occurrence of overt disease.

Noe, Greene and Cheney[6] observed that patients, previously on suppressive quinacrine therapy, who have their first attack of malaria in this country show a tendency to run the complete two-year to three-year relapsing course of the disease. Should this patient show a similar tendency, and particularly if he is treated only with quinacrine, he might well suffer a malarial relapse as long as four or five years after his last exposure in the Southwest Pacific. This implies that physicians must continue to consider the possibility of malaria in febrile illnesses in veterans. The future experience of the

armed forces and the Veterans Administration will be of help in clarifying this problem, just as use of the new antimalarial drugs[15, 16] offers hope of its eventual solution.

Summary

A primary attack of vivax malaria occurring in an ex-serviceman twenty-seven months after his last exposure in an endemic area is reported.

Such prolonged latent periods have not been reported in natural malaria. Primary attacks occurring eighteen months after discontinuance of quinacrine suppression have been observed, and the effect of this drug is suggested as a possible explanation for the delayed attack in this patient. If this, or similar cases, show a tendency to further relapses, it would indicate that a small number of malarial relapses may continue to occur for four to five years after the return of the last serviceman from endemic areas in the Southwest Pacific.

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MEDICAL PROGRESS

PROCTOLOGY

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IN a comprehensive bibliography prepared for the 1947 meeting of the American Proctologic Society numerous articles on nonmalignant and malignant lesions of the colon and rectum, published during 1946, were carefully listed and indexed, and some of them abstracted in greater or less detail. With perhaps an equal number in the literature of 1947, it is apparent that a complete review of them is a task too extensive for inclusion in this rather short article. Spectacular advances in this field are the exception, — not the rule, — and yet articles of value and interest, contributed both by those who limit their work to proctology and by those who do not, have appeared from time to time.

The American Proctologic Society, organized in 1899 and holding yearly meetings since that time, has always published its papers in a series of bound volumes entitled *Transactions of the American Proctologic Society*, until this year. The February, 1948, issue of the *American Journal of Surgery* was devoted exclusively to publication of the papers read at the 1947 meeting of the society.

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At this meeting, a paper by Courtney,[1] was given the Hermance award as being the best original paper presented on that occasion. Courtney reported the results of a study carried out in the anatomic laboratories of the Graduate School of the University of Pennsylvania, under supervision of Professor Batson of the Anatomy Department, in an effort further to clarify the classification and mode of extension of perirectal abscesses. Eight cadavers were dissected in detail, and 40 cadavers were inspected while being dissected by others, both from above and below, and with the aid of sagittal, parasagittal and coronal sections.

Heretofore there have been described, and accepted as accurate, three deep spaces, — the retrorectal and the right and left pelvirectal spaces, — abscesses of which are recognized.

As a result of this study Courtney has identified a fourth deep space, to which he has given the name "posterior levator space." This space is formed by a division, close to the rectum, of the levator muscle attachment into a superior and inferior layer, which produces a V-shaped flare with attachments at

different levels to the longitudinal muscle fibers of the rectum, thus creating a space, bounded by the longitudinal muscle of the rectum medially, by the superior and inferior muscle bundles of the levator above and below, and extending around the posterior surface of the rectum from side to side, decreasing in size and depth as the pubis is approached, and with its greatest size near the posterior midline.

Infection of this space arises by upward extension from one of the posterior crypts, and is characterized by formation of a deep abscess, not palpable externally but felt as a rounded swelling on intrarectal palpation in the posterior midline.

Courtney advises incision in the midline posterior to the anus, spreading the fibers of the sphincter as they converge toward the coccyx. If the abscess has spread laterally a counterincision can be made lateral to the sphincter and as far forward as necessary.

Parasympathetic Supply of the Distal Colon

On the basis of a dissection of 9 infant and 9 adult bodies, Lannon and Weller[2] found variations in parasympathetic distribution in practically every body, and in the two sides of any one body. On the left, the pelvic autonomic fibers usually arise from the anterior aspect of the second and third sacral nerves within 1 cm. of their exit from the anterior sacral foramens. Well defined fibers pass anteriorly as the nervi erigentes, and from three to six moderately thick strands pass medially, upward and anteriorly, to the distal colon. The nerves are creamy white, and a tiny red blood vessel can be seen on the surface of the nerve — an identifying characteristic. Difficulty was encountered in tracing the fibers through the dense pelvic fascia, but it was possible to identify them in some of the dissections as giving off some fibers to the rectum just after piercing the fascia, the remainder passing down with the superior hemorrhoidal artery.

There was also found to be a connection of some fibers on the left with the inferior hypogastric plexus. At the level of the promontory the fibers leave the artery and pass across the left common iliac artery and upward into the mesentery of the bowel, where some fibers could be traced to the bowel itself as high as the midportion of the descending colon. They do not enter the bowel with the vessels, but independently.

On the right side the plan is similar in general except that the nerves tend to lie at a distance from the superior hemorrhoidal artery and in closer association with the inferior hypogastric plexus.

The authors believe that they have demonstrated several points of clinical interest: that in resections of the rectum and pelvic colon the parasympathetic vessels are bound to be destroyed — a fact that has always been considered to be true. On the other hand a periarterial stripping of the inferior mesenteric artery and presacral neurectomy should not interfere with the parasympathetic supply to any part of the colon, but in a high colonic resection the part of the colon lying above the point of resection and below the distal point of vagal parasympathetic supply will be deprived of its parasympathetic supply.

Anorectal and Urinary Dysfunction

McCrae[3] discusses the intimate relation between anorectal and urinary dysfunctions on the basis of the common blood supply and innervation of the two areas. The bladder and the anorectum both originate from the fetal cloaca in their embryologic stage. Each is supplied with blood from the hypogastric artery by its various branches, though the rectum also receives some of its blood by way of the superior hemorrhoidal artery from the inferior mesenteric.

Each organ is likewise innervated by the somatic, sympathetic and parasympathetic systems. Somatic supply is by way of the pudendal nerve from the second, third and fourth sacral vessels. It is through this nerve that the voluntary impulses of urination are carried. Another branch of the pudendal, the inferior hemorrhoidal nerve, supplies the anal region. The pudendal nerve is both motor and sensory and on this fact is best explained the retention of urine following hemorrhoidectomy and other anal procedures, owing to a reflex contraction of the external vesical sphincter following trauma to the perineal branch of the pudendal nerve.

Perforations of the Colon

Andresen[4] has gathered some interesting facts regarding perforations of the bowel during proctoscopy. His figures are based on 215 replies to questionnaires sent to 340 members of the American Gastro-Enterological Association and the American Proctologic Society. From 34 of these replies he received reports of 46 cases of perforation, which he has analyzed.

Onset with sudden pain occurred in only 26 patients (55 per cent).

Diagnosis was made by direct observation through the proctoscope in 25 cases (54 per cent).

In the 46 cases 21 patients had no other disease of sigmoid or rectum. There were 13 carcinomas, 5 others with diverticula in the sigmoid, 3 with ulcerative colitis, 2 with polyps, 1 with lymphopathia venereum, and 1 with hemorrhoids only. Nineteen patients, or 41 per cent, died, including the 3 patients who were not operated on.

Immediate operation showed a mortality of 8 per cent, and when operation was delayed one to six hours the mortality was 32 per cent, from six to twelve hours, 50 per cent, and over twelve hours 75 per cent.

The best results were obtained in 8 cases in which colostomy was performed, 2 with suture and 6

without suture of the perforation. Only 1 of the 8 patients died. In 23 cases in which the perforation was closed, but colostomy not done, there were 6 deaths. Of 22 patients not operated upon, in the two series of cases, there were 13 deaths (59 per cent). Nine recovered.

The over-all mortality in the 94 cases was 47 per cent. Andresen emphasizes the importance of passing a proctoscope only under direct vision, and discontinuing the attempt if poor preparation, bleeding, spasm and so forth make it impossible to obtain a good view.

I should like to urge, in addition to these precautions, that proctoscopic examinations not be made on patients under anesthesia, and in lithotomy position, if they can be avoided. More information can be obtained, and with less risk, if proctoscopy is performed with the patient in the inverted, or in the knee-shoulder position, prior to anesthesia.

Davis[5] reports 3 cases in which an enema tube, inserted through a colostomy stoma, perforated the sigmoid and permitted the enema fluid to enter the peritoneal cavity. In 1 case immediate pain brought the patient to operation within 6 hours, and in the second case after three days, with signs of peritonitis, whereas the third patient was operated upon after three weeks with drainage of an abscess. All recovered.

This is an unusual occurrence though it has also happened in 2 of my patients who were taking their own enemas. In 1, who had had for some time a colostomy for lymphopathia venerea with extensive rectal involvement, the perforation produced sudden pain with ensuing tenderness at one side of the stoma, but no fluid had been introduced and operation was never necessary, the small cavity, demonstrated by barium enema a little later, eventually obliterating itself. My second patient came into the hospital with fever, distention and cramps, suggesting small-bowel obstruction. After some decompression had been obtained with a Miller–Abbott tube, pus could be seen coming from the colostomy in small amount, the abscess having drained itself into the bowel. In this case a colostomy was constructed at a higher point in the colon.

Pilonidal Cyst and Sinuses

Pilonidal-sinus problems seem to fall within the scope of this review by virtue of the proximity of the lesions to the anus and the natural gravitation of many of these patients to the offices and clinics of surgeons doing proctologic work. Throughout the war, efforts were directed toward developing improved methods of reducing the healing period following operation, mostly by the use of primary closure in one form or another. Many ways of accomplishing this have been described, and series of cases published, with more or less follow-up data, since Lahey described his method of sliding a flap of skin, fat and fascia to the midline to fill in this poorly healing area.

Pope[6] has reported a considerable experience at the Chelsea Naval Hospital with an operation that he devised, the principal feature of which is the sliding of a single mobilized section of gluteus muscle across the midline to obliterate the defect following excision of cyst and sinuses. In 92 cases out of a series of 130, this operation was used, whereas 38 others were closed by primary suture without use of the sliding muscle graft. Follow-up data were reserved for a subsequent article, but the results, so far as could be observed during the extended hospitalization often given to Army and Navy personnel, were very good.

Success in achieving primary healing in pilonidal cyst excisions depends upon: bacteriologic cleanliness of the lesion at time of operation; careful hemostasis and tissue handling; obliteration of dead space in the suturing process; and careful postoperative treatment, including chemotherapy.

It is obvious, therefore, that good results will depend upon proper selection of patients, the use of a procedure best suited to the individual case, and upon the ability of the individual surgeon to carry through on the technical procedure and aftercare. The open method still remains the most certain to produce a permanent healing.

Fistula

The old idea that most anal fistulas are tuberculous is once again refuted by a study that Jackman and Buie[7] carried out in 600 patients with anal fistula. Of these only 11.5 per cent showed evidence of tuberculosis anywhere in the body, and in only 7 or 8 per cent was the fistula itself proved to be tuberculous. There was no case of tuberculous fistula in a person who did not have tuberculosis elsewhere in the body. These authors consider the guinea-pig inoculation with material from the fistula to be the best test of the nature of the fistula, though they admit that contamination of the area could occur from higher up in cases in which the histology of the fistula is negative for tuberculosis.

Skir[8] has studied various reports in the literature, totaling 50 cases, in which carcinoma was considered to have developed from a previously existing fistula. From this group he has selected 14 in which the fistula was known to have been present for at least ten years prior to the diagnosis of cancer, thereby strengthening the likelihood that the cancer really did supervene on the fistula. To this group of 14 he adds 3 from the Brooklyn Hospital. These 3 patients were elderly people, 2 of them Negroes, all with long histories of fistula — ten, thirty and fifty-five years of intermittent discharging sinus — and all presenting a similar picture: that of a fungating, ulcerating tumor protruding from the fistulous buttock, through the skin of which it had ulcerated. The pathological reports were

all "mucinous carcinoma." The fact that 2 of Skir's 3 patients were Negroes is also of interest because of the very low incidence of cancer of the rectum and anus in that race, as borne out by the experience of other men whose hospital clinics have a large Negro attendance.

These reports are of value, and presumably the occasional development of carcinoma at the site of a chronic fistula of long duration may be considered to bear a relation to the chronic irritation of the long-continued infectious process. If there is a direct relation these cases can be considered as demonstrating a good reason for dealing with fistulas reasonably promptly and eradicating them. However, it seems unnecessary to resort to the fear of cancer as an argument in convincing people that their fistulas should be operated upon when the obvious inconvenience and discomfort of recurring abscesses and of intermittent or continuous drainage are sufficient reasons for instituting surgical treatment promptly.

Kenney[9] reports his experience with a method of excision and suture of anal fistulas, carried out in 12 cases with healing in 11 and with no recurrences for follow-up periods extending from two to six months. After a preoperative preparation with sulfanilamide and castor oil he carefully cuts around the external opening, after first passing a probe through the sinus, and then incises radially toward the anus but not into the tract and not across the mucocutaneous junction. The sinus is dissected out, free of the muscle, after which the internal opening is encircled and the sinus removed. The tissues are then infiltrated with penicillin solution, using 20 to 100 cc. of a solution containing 2000 units per cubic centimeter and after careful hemostasis the wound is obliterated with fine cotton sutures in layers, the internal opening closed with fine chromic and the external opening with 80-gauge or 120-gauge cotton. Patients leave the hospital in several days.

This is a praiseworthy attempt to improve the technic of dealing with anal fistula, and is in line with the advances made in primary union after pilonidal-sinus excisions. It is perhaps only fair, however, to emphasize the difficulties encountered by many surgeons in attempts to obtain primary healing in the anal area, and it is probable that most surgeons will have a higher percentage of cures if they adhere to open incision and drainage operations.

Pruritus Ani

Attempts to relieve or cure pruritus of the anal region have embraced as wide a variety of therapeutic agents and methods as any pathologic condition, and yet no striking progress has been made in establishing its cause or in finding a permanent cure.

Frankfeldt[10] calls attention to the well known fact that the majority of people with hemorrhoids, fissures, fistulas, incontinent sphincter, colitis and so forth do not complain of itching despite the fecal soiling, mucus and purulent discharge that often accompany these conditions. Therefore, it seems to him logical to assume that two factors operate in people who have pruritus ani: a sensitization of the skin, and an irritant (allergen or antigen). With this premise he concludes that anal pruritus must be an *allergic manifestation*.

A careful history, dealing with all sorts of factors that might contribute to the establishment of an allergy, is taken from each patient by means of an extensive questionnaire, and as a result Frankfeldt believes that he can classify the cases into five groups, allergic to food, fungus and bacteria, contact dermatitis, drugs and atopans.

In mentioning the various substances to which an allergy might exist Frankfeldt presents a list so long that it is hard to see how anyone could escape having pruritus.

He believes that histamine is in some way concerned with the problem and has employed the antihistaminic agent, pyribenzamine, in treatment, giving 50 to 150 mg. after each meal and at 10 p.m. This plan was carried out in 90 patients with 85 to 100 per cent relief from itching in 57. Of the 57 he considered 26 to have a food allergy, 10 a fungus allergy, 12 contact dermatitis, 6 a drug allergy, and 3 an atopic dermatitis. An ointment of 2 per cent pyribenzamine in a water-washable base was also used in 11 cases, with relief only in patients who had also experienced relief from oral administration of the drugs. In 33 patients there was no relief.

Instructions regarding hygienic measures were given to the patients in all cases.

In discussion of this paper Belknap reported only 13 per cent good results in his experience with pyribenzamine, whereas Terrell emphasized the role of fungi as of prime importance.

All in all proctologists are not much farther along toward a cure of pruritus ani than they were thirty years ago.

Kallet[11] reports gratifying relief in 92 per cent of 100 cases of intractable pruritus ani subjected to a combined excision and under-cutting operation, which he calls "the clover-leaf operation" because of the appearance of the area following excision of three or four elliptical segments of perianal skin. Patients selected for this procedure were all chronic cases with symptoms of long duration — up to twenty years. Most of them had had various types of treatment — such as ointments, x-rays, injections and other rectal surgery. The operation is best suited to patients with localized thickening, skin folds, lichenification and hypertrophy of the perianal skin.

The incisions are made only up to the anal verge, not into it, and strips of skin about 0.6 cm. wide are left between the elliptical incisions. These bands

are then undercut. Complete closure of the wounds occurs in about a month, and Kallet advises digital dilatations of the anus periodically.

The difference between this procedure and the old undercutting operation, as advocated by Ball, lies in the excision of skin that characterizes the former, whereas in the latter little or no skin is sacrificed.

Discussion of this paper brought forth varying reactions, including emphasis on the value of subcutaneous alcohol injection as a substitute for too radical excision of skin and mention of the value of including some degree of anal-canal surgery — removal of papillae and crypts, and partial incision of the anal ring to relieve tightness — in association with the external work. Kallet, in closing the discussion, strongly urged that no intra-anal cutting be done and emphasized that in most of these cases the anal canal is found to be quite normal. In the last statement I agree with him.

Hemostatic Agents

Rosser[12] reported, as an experimental study in 141 anorectal operations, the use of gelatin sponge (gel foam), oxidized cotton or oxidized gauze as a packing in the wounds at time of operation. Fibrin foam was not tried because of its origin in human blood, which might make it less available. Rosser cites the experimental work of several authors indicating that gelatin sponge is nonirritating and gradually absorbable. He used it in 43 anorectal wounds and found that it usually disappeared in forty-eight hours, though in large surface wounds it remained four days.

Oxidized gauze and cotton were used in 98 cases, the best results being obtained with small pieces placed directly in the cuts. Hemostasis was aided, and the material liquefied readily so that it did not occlude drainage. Rosser used these materials in most of the common types of anal operations as well as in pilonidal wounds.

It is probably superfluous to add a word of emphasis, with which Rosser would be the first to agree, that the above devices are not a substitute, but only an adjunct to careful ligation of bleeding points, particularly arterial bleeders.

Relief of Pain

Mentzer[13] employed the oil anesthetic "anucaine" in 1510 cases, with satisfactory relief of postoperative pain and a decrease in the number of patients requiring catheterization. This particular preparation contains 0.5 per cent procaine, 1 per cent butesin, 5 per cent anesthesin, 5 per cent benzyl alcohol and as much sweet almond oil as necessary. The solution was injected through three points of entry, 2.5 cm. to the right and left of the anus and directly posterior to it, 2.5 to 5 cc. being placed in each lateral area and 5 cc. posteriorly. The solution was injected at three levels — subcutaneously, into the external sphincter and into the levator-muscle attachment. An average hospital stay of only four days and definite decrease in pain were attributed to the use of this preparation.

Prolapse of the Rectum

Hayden[14] reviewed the experience at the Massachusetts General Hospital with the surgical treatment of complete rectal prolapse over a thirty-four-year-period (1912 through 1946), with such follow-up data as could be obtained. During this period 60 patients were operated upon one or more times by 23 different surgeons, utilizing nine or ten different procedures in various combinations. The largest number of patients operated by one surgeon was 18, and the next largest 9, and so on down the line, illustrating the fact that anyone's experience is bound to be limited in this condition, which is not encountered with great frequency. The Moschcowitz operation (obliteration of the cul-de-sac of Douglas) was used, alone or in combination with other procedures, in 43 cases. Other procedures consisted of fixation of uterus or of cervical stump, suspension of uterus or cervical stump, Mikulicz resection of sigmoid or simple fixation of sigmoid to left lateral pelvic wall, posterior fixation of rectum by various methods — Lockhart-Mummery, Tuttle and Maes-Rives — DeLorme, amputation of the prolapse by surgical excision or by compression ligature and, finally, linear cauterization. Good and poor results were obtained by most of these methods, some of the best results being achieved by combined procedures. The Moschcowitz operation, with or without modifications or additions, is based on a sound conception of the underlying disease, and good results may be expected, also, from use of the DeLorme operation and by excision of the prolapse.

Hayes and Burr,[15] in reporting on 9 cases of complete rectal prolapse seen in a period of 9 years, have concluded that the procedure advocated by Graham in 1942, with a modification of their own, is an eminently satisfactory way of dealing with this condition. Graham's procedure includes an incision of the pelvic peritoneum and freeing of the rectum anteriorly and posteriorly as in abdominoperineal resection for cancer. The levators are then sutured together anteriorly. Hayes and Burr modified this in 1 case by suturing the lateral ligaments across in front of the rectum, thus taking up their slack. Then, with the pelvic portion of the colon held taut, the excess peritoneum was infolded and sutured around the rectum, thus obliterating the previously deep cul-de-sac. A new bed for the sigmoid was then created by incising the lateral parietal peritoneum for 10 or 12 cm. and anchoring the taut sigmoid to the peritoneal edges raised from the deeper tissues.

Dunphy,[16] sharing the dissatisfaction of most surgeons about the treatment of complete prolapse, has utilized a combined abdominal and perineal

operation in 4 patients, with satisfaction to the patients and to himself though the follow-up period had not exceeded a year and eight months in any of the 4 at the time he wrote the paper. The operation described combines the best features of several of the radical procedures previously in use and is done in two stages — the perineal part first. It embraces circular amputation of the external prolapse, excision of the peritoneal hernial sac so far as accessible from below, suture of the levators anteriorly, and reconstruction of the lumen of the bowel by a combination of interrupted and short continuous sutures, to eliminate or reduce the degree of narrowing at the suture line.

A week of preliminary preparation with sulfathaladine to diminish the bacterial flora in the bowel is advocated, and during this time, also, the patient is encouraged to build up sphincter tone by numerous voluntary contractions of the muscle — "a thousand times a day."

Some days later the abdomen is opened and the rectum mobilized as in the abdominoperineal resection for cancer, after which some deep sutures are placed laterally, including peritoneum and fascia and lateral ligaments. The cul-de-sac is then obliterated by pursestring sutures, as in the Moschcowitz operation, and the pelvic portion of the colon anchored to the lateral wall of the pelvis with interrupted silk sutures.

Colitis

Although the etiology of ulcerative colitis is still unknown, various experiments in the treatment of the disease continue to be reported in the literature. Gill[17] has utilized mucosa from the small intestine, particularly the jejunum, of pigs, on the theory that ulcerative colitis may be due to a deficiency of some constituent normally supplied by the mucosa of the small intestine. The mucosa is given in the form of a desiccated raw preparation, one ounce (equivalent to one pound of the original mucosa) being given daily.

Nasio[18] has utilized a colloidal preparation similar to the intestinal juices, giving it by the drip method.

Alvarez[19] emphasizes the value of amino acid therapy in ulcerative colitis to make up for the loss of protein in the evacuations.

Kiefer and Jordan[20] presented before the American Proctologic Society an analysis of 430 cases of ulcerative colitis from the Lahey Clinic. Mention was made of the psychosomatic factor in this disease, of the unexplainable remissions and exacerbations and of its characteristic proctoscopic picture.

The proctologic complications occurring in this series consisted of perianal abscess in 12 per cent of cases, 14 strictures, 5 severe perianal skin infections and 25 cases of accompanying hemorrhoids or fissures. The authors also stated that hemorrhoidectomy had been performed in a good many cases before they came to the clinic, presumably by surgeons who were not aware of the true diagnosis.

Adenocarcinoma developed in 7 per cent of the long-standing cases, possibly superimposed on true polyps that existed coincidentally.

In the 430 cases, the rectum alone was involved in 73, or 17 per cent. Involvement of rectum and part or all of the left portion of the colon occurred in 92 cases, or 21 per cent, and in 242 cases, or 56 per cent, the right portion of the colon was also involved. A fourth group — cases with segmental colitis and no rectal involvement — numbered 23, or 6 per cent. Medical measures in treatment were designed to control diarrhea, malnutrition, blood loss and anemia and sepsis. Emphasis was laid on the term "control" rather than "cure" — a distinction with which all agree in the management of this disease.

In the milder cases fever therapy, by means of gradually increasing doses of typhoid vaccine, has been used with gratifying results, and the elimination of causes of psychic trauma is desirable if possible.

Medical treatment in 34 cases with proctitis alone resulted in control of the disease that was good in 16, fair in 9 and poor in 9. Of 84 cases involving only the descending colon good control was obtained in 22, fair in 13 and poor in 28. In the group with generalized colitis (160 patients) the results were as follows: good control in 37, fair in 11 and poor in 77, whereas in the segmental group of 14 cases good control of the disease resulted in 5, fair in none and poor in 6.

With their experience of obtaining distinct improvement in most patients after ileostomy the authors believe that to delay this measure over a week in a patient with spiking temperature and evidence of increasing toxicity is a very risky postponement.

There were 32 "emergency" ileostomies performed, with 75 per cent mortality. For this reason every attempt is made to anticipate the need for ileostomy to avoid the necessity for an emergency procedure in a poor-risk patient. Elective ileostomy in 76 patients yielded a mortality of only 6.5 per cent.

Partial or complete colectomy was performed in 93 patients —a total of 146 different procedures — with an operative mortality of 8.2 per cent and a case mortality of 12.8 per cent.

The König–Rutzen bag is considered to be the best appliance for ileostomy control, since it is cemented to the skin and if properly applied can be made leak tight both day and night.

Polyps

Binkley and Sunderland[21] classify benign adenomas of the colon as areas of hyperplasia, adenomas and papillary adenomas — the second group

being most frequently encountered. Emphasis is laid on the uncertainty of pathological diagnosis in some cases owing to the fact that early malignant change in a small area may be easily overlooked. The importance of recognizing clinically the characteristics of malignant change is also stressed — the induration, ulceration and bleeding on slight trauma and the color of the lesion. Treatment varies with size and location of the lesion — surgical excision, removal with a snare or electrocoagulation. Radiation is reserved for the polyps that cannot be completely removed, and can be given either by external application of x-rays or by intrarectal application of radium to the surface of the lesion or in the form of gold radon seeds. Once in a while the rectum must be removed completely to eradicate a lesion, particularly if the base is suspicious of cancer.

Swinton[22] reported the presence of polyps in the colons of 311 of 1843 patients coming to autopsy at the New England Deaconess Hospital. In 42 of the 311 there were multiple lesions. Over 50 per cent were within reach of a 25-cm. sigmoidoscope.

Of 22 cases reported in this paper, very early malignant change in the polyp but not involving the stalk was found in 12 cases, and a local removal was performed. All patients had had bleeding as a symptom. Two of these also had a later radical operation, but no cancer could be found in the specimens. Of the group, 10 had tumors in the colon — 8 in the sigmoid and 2 in the descending colon.

In 41 cases with polyps, removal was accomplished by the abdominal route. There was no evidence of malignant change in 31 of these. Bleeding was a symptom in 38 of the 41 cases. One death occurred.

270 Commonwealth Avenue

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

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CASE 34371

PRESENTATION OF CASE

A thirty-year-old man was admitted to the hospital because of epigastric distress.

The patient had previously been well until one year prior to admission, when he began to notice epigastric distress following large meals. This became gradually more persistent and then became consistently associated with the noonday meal. X-ray studies done at another hospital four months before entry showed a filling defect on the greater-curvature side of the pars media of the stomach surrounded by exaggerated rugae and a suspicious ulcer crater in the center of the area. Three days later a repeat examination failed to show any filling defect but there were some hypertrophied rugae on the greater curvature. Further studies one month before admission again demonstrated a questionable gastric lesion and a total achlorhydria following an alcohol test meal. He was given dilute hydrochloric acid, but the symptoms continued. There was no relation of the distress to fatty or other particular foods, and alkalies afforded no relief. Neither did eating smaller meals bring any relief from the gastric distress. He gained several pounds over the several weeks before entry. There was no change in bowel habit.

The past history and a system review were noncontributory.

Physical examination revealed a well developed and well nourished man in no distress. Examination of the lungs, heart and abdomen was entirely negative.

The blood pressure was 120 systolic, 65 diastolic.

Examination of the blood disclosed a white-cell count of 8000. The hemoglobin was 13.8 gm. per 100 cc. The urine was normal. Gastric analysis after an alcohol test meal showed no free hydrochloric acid in the fasting, half-hour and one-hour specimens. All three were guaiac positive. A gastrointestinal series demonstrated a normal esophagus. The stomach was situated high and transversely. Unusually large rugal folds were present in the proximal half of the stomach. The mucosal pattern of the distal portion of the stomach was not abnormal, although slight mucosal thickening was possibly present. The mucosa in the upper half appeared to be coated with foreign material, and the pattern was mottled. The walls of the stomach were pliable. The duodenal bulb was not remarkable.

Gastroscopy was done, and the gastroscope readily passed. The angulus was somewhat rigid, and no peristalsis was seen. There was not the usual response to air inflation. Only the proximal portion of the antrum was visualized, and the distal antrum and pylorus were not seen. Throughout the body of the stomach, particularly on the posterior wall and greater curvature, the rugae were very thick and tortuous. The wall of the stomach was also somewhat rigid and did not respond to air inflation. The mucosa was markedly hemorrhagic throughout the body of the stomach and bright-red blood apparently oozed from the posterior wall and greater curvature. A similar appearance was present to a lesser extent on the lesser curvature. At times there appeared to be an inconstant, round, submucosal mass on the greater curvature in the lower part of the body of the stomach.

Following these diagnostic procedures an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. JAMES A. HALSTED: I should like to ask Dr. Allen about this man's total weight loss. It is not clear.

DR. ARTHUR W. ALLEN: It is my impression that he had regained all the weight he had lost before he came to operation.

DR. HALSTED: In other words, he had a year's symptoms without any essential weight loss.

DR. ALLEN: He was certainly well nourished at the time of operation.

DR. HALSTED: Is there any record of a stool examination?

DR. ALLEN: The stools were guaiac negative.

DR. HALSTED: During gastroscopy, "there was not the usual response to air inflation." I believe that refers to the fact that with the usual response one might expect peristalsis to develop as a result of inflating the stomach. The fact that the pylorus was not seen is not surprising. In 50 per cent of gastroscopies one cannot see the pylorus.

Are the x-ray films available?

DR. JAMES MCCORT: This examination shows the widening of the rugal folds, which appears mainly in the fundus of the stomach, extending down into the body of the stomach. According to the fluoroscopist's note, he was able to discover no rigidity or loss of pliability by palpation.

DR. HALSTED: The lower end is normal?

DR. MCCORT: The rugal pattern in the lower end of the stomach is not altered.

DR. HALSTED: The x-ray findings suggest gastritis, but the x-ray diagnosis of gastritis is not accurate. One can see apparent gastritis on x-ray examination and find a normal-appearing mucosa by gastroscopy, but the reverse is more generally true — that the x-ray film appears normal and gastroscopy demonstrates gastritis.

In summary, this man had a chief complaint of chronic epigastric distress for a year, with no anemia and no weight loss. There was evidence of bleeding by gastroscopy as well as by examination of fluid removed from the stomach by aspiration. Apparently he had a rather diffuse lesion that tended to involve the upper part of the stomach. This was first reported from another hospital four months before entry here. At that time he showed what was thought to be an ulcer crater in the center of the area.

From the evidence at hand it is not possible to make more than a guess at the diagnosis in this patient without surgical exploration. What are the differential possibilities? The commonest lesion that causes chronic epigastric distress at this age is peptic ulcer. I rule that out because of the achlorhydria, confirmed by two examinations and the history. Such rare lesions as tuberculosis and syphilis, which might involve the stomach, can also be discarded, since there was no evidence of these diseases elsewhere in the body. We come down to a tumor or gastritis. If it was a tumor, was it cancer or a lymphoblastoma type of tumor or possibly a benign tumor? Carcinoma is about a hundred times more common in the stomach than lymphosarcoma statistically. At this patient's age, however, it is only about fifteen times more common. Cancer of the stomach is more apt to be in the lower end; 50 per cent of cases involve the antrum and pylorus. This lesion apparently involved the upper portion of the stomach, which makes one suspect more strongly some other lesion than cancer. If he had carcinoma, with symptoms of a year's duration and with this rather extensive involvement as evidenced by gastroscopy, I should expect that he would have lost weight and be definitely anemic; neither weight loss nor anemia was mentioned, so that I should be in favor of tumor other than carcinoma, provided it was a tumor.

Could it have been gastritis? A severe hypertrophic ulcerating type of gastritis can produce this picture, both by x-ray and gastroscopic findings as well as clinically. I cannot interpret the gastroscopy; it is a subjective method of examination, and I have to rely on what the gastroscopist thought at the time. I do not imagine a biopsy was taken; there is no mention, although it is now possible to take biopsies through a new kind of flexible gastroscope. I do not know what Dr. Benedict's results have been with that instrument. The achlorhydria is an important finding here. At the age of thirty, it is estimated to occur in 2 to 4 per cent of people normally. Thus the achlorhydria in a patient of thirty would almost surely be due to disease. Schindler[1] says that gastritis is not associated with achlorhydria as a rule; the hypertrophic type is generally associated with acid.

The suggestion of a mass that the gastroscopist reported — apparently a round mass protruding from the submucosa — may be important and suggests that this man had a tumor of the upper part of the stomach, not a carcinoma. Hodgkin's disease, restricted to the stomach and not involving other parts of the gastrointestinal tract or other parts of the body, is extremely rare. There were only 20 cases reported up to 1946. The same observation is true of leukemic infiltration of the stomach in an aleukemic phase of the disease. I would have to rule this out without any other evidence of the disease. There is nothing to suggest that this was an extragastric tumor, such as retroperitoneal sarcoma, which was compressing or invading the stomach. No mass was felt, and the x-ray report indicates that the lesion involved the stomach wall. Leiomyoma or leiomyosarcoma is usually an isolated tumor, although in rare cases it has been reported as a diffuse tumor involving the stomach. This type of tumor characteristically is without symptoms except for bouts of massive bleeding, with no digestive symptoms of pain and distress. Lymphosarcoma comprises about 40 per cent of gastric sarcomas. This may diffusely involve the stomach or may grow inward or outward as a discrete tumor.

I suppose, on statistical grounds alone, that carcinoma is perhaps the most likely diagnosis, but for the reasons I have given, I do not believe it was present. This could have been extensive hypertrophic gastritis or a lymphomatous or sarcomatous type of tumor. Gastritis is much more common, but because of the achlorhydria and the gastroscopic findings this case is more suggestive of a diffusely invading tumor, probably lymphosarcoma.

DR. BENJAMIN CASTLEMAN: Will you tell us what your opinion was before operation, Dr. Allen?

DR. ALLEN: Dr. Halsted has covered our line of reasoning very accurately. We were not sure that this man had a serious lesion of the stomach, but we felt that we had to explore him to find out whether there was tumor in the stomach or not. This was based to some extent on the achlorhydria and on the gastroscopic impression. We had had an almost identical picture in a patient who proved to have a lymphoma of the stomach. We have also had 2 other cases presenting the same picture but with acid in the stomach that proved to be due to giant gastritis. In these patients there was an enormous increase in the size of the rugae of the stomach.

I explored this patient with an open mind, thinking that I would have to rule out a serious surgical situation.

Clinical Diagnosis

Gastric tumor.

Dr. Halsted's Diagnosis

Lymphosarcoma of stomach.

Anatomical Diagnosis

Chronic gastritis, superficial type, superimposed on hypertrophic type.

Pathological Discussion

Dr. Allen: At operation the stomach was, as you can see, very high and difficult to palpate. This man was quite fat. Not being satisfied with palpation of the stomach from the outside, I opened the anterior wall of the stomach and put one hand inside the stomach and with my other hand outside I could feel the entire stomach throughout and be sure that the patient had no tumor. He did have huge rugae, and we took out a section, perhaps not so high as we would have liked but high enough we thought to include a portion that would be diagnostic. The stomach was then closed, and the abdomen closed — just a biopsy was done.

Dr. Castleman: The microscopical sections showed a definite and characteristic chronic gastritis. Normally the glands in the fundic portion of the stomach are composed of cells whose nucleus is basally situated, the rest of the cell being filled with large amounts of mucin. Also, in the normal stomach there is a variably cellular infiltration of plasma cells, lymphocytes and eosinophils between and in the glands in the neck zone of the mucosa. Some years ago Drs. Benedict and Mallory[2] reviewed our gastric material and determined about how much cellular infiltration in the various parts of the stomach was within physiologic limits.

In this particular case, instead of the normal type of epithelium, the glands had lost their mucin secretion, the cells were smaller, and the cytoplasm was dense. Function was obviously disturbed. There was an intense cellular infiltration, polymorphonuclears predominating, involving the upper part of the mucosa, much more than is seen normally. This form of gastritis is called superficial gastritis, and it may be superimposed on the hypertrophic or atrophic form. I believe that this is an example of acute and chronic gastritis of the superficial type superimposed on the hypertrophic form.

Dr. Halsted: According to Schindler[1] the superficial type of gastritis is much more commonly associated with achlorhydria than the chronic hypertrophic gastritis; that is probably the explanation of the achlorhydria in this case.

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CASE 34372

Presentation of Case

A seventy-year-old retired merchant entered the hospital on his physician's advice following x-ray studies revealing a mass in the right lung.

For the past fourteen years the patient had had frequent checkups for a cardiac condition, although his only symptom was slight exertional dyspnea. He had noticed no edema, orthopnea or weakness, but had been told a few years previously that his blood pressure was low. One year previous to admission a routine chest x-ray film revealed a mass in the right lung. Five months later x-ray study showed essentially the same picture, but in an examination two months prior to admission a slight change in the mass was noted and he was referred here. During the past year he had been asymptomatic, with no weight loss, chest pain, fever or remarkable upper respiratory infection. During this time cytologic smears of the sputum were twice reported negative.

Fifteen years prior to admission an enucleation of the left eye had been done for a malignant melanoma. About ten years prior to entry he had received injections for "calf pains."

Physical examination revealed a heart enlarged to the upper limit of normal. A long systolic and a short diastolic murmur, not widely transmitted, were heard in the aortic area. The peripheral pulses were of the Corrigan type.

The blood pressure was 200 systolic, 65 diastolic.

Examination of the blood disclosed a hemoglobin of 15.8 gm. and a white-cell count of 7600, with 61 per cent neutrophils, 26 per cent lymphocytes, 6 per cent monocytes and 4 per cent eosinophils. A urinalysis was negative. The serum nonprotein nitrogen was 33 mg., and the protein 7 gm. per 100 cc. A cytologic smear of the sputum was negative. Blood Hinton and Wassermann tests were positive.

X-ray films of the chest showed a slightly lobulated mass of homogeneous increased density within the posterior segment of the right upper lobe overlying the right fifth, sixth and seventh ribs posteriorly. The mass was approximately 5 cm. in diameter; although it lay against the posterior wall there was no evidence of erosion. The heart was somewhat prominent in the region of the left ventricle, and the aorta was tortuous. There were areas of calcification in the mediastinum. Intravenous pyelogram showed prompt excretion in fair concentration, outlining grossly normal-appearing calyxes, pelves and ureters. The bladder shadow was not remarkable. There was opaque material in both buttocks. The bones of the pelvis and lumbar spine were not remarkable. An electrocardiogram was consistent with left ventricular strain and hypertrophy.

On the eighth hospital day an operation was performed.

Differential Diagnosis

Dr. Earle M. Chapman: I think we should start out by seeing the x-ray films.

Dr. Stanley M. Wyman: The mass described is well seen in the right-upper-lung field in the posteroanterior view, lying far posteriorly, and not very well seen in the lateral film. The heart shadow is definitely enlarged, probably chiefly left ventricular, and the aorta is tortuous as described. The pulmonary vascular shadows are, I think, slightly increased in prominence, suggesting some vascular engorgement. There is no evidence of rib erosion and no evidence of involvement of the chest wall itself.

Dr. Chapman: The pyelograms were done to exclude kidney tumor, I assume.

Dr. Wyman: The kidneys seem to be normal. The calyceal pattern shows no abnormality. The bladder shadow is not included on the film. This is the opaque material in both buttocks.

Dr. Chapman: There is no osteoporosis?

Dr. Wyman: Nothing significant.

Dr. Chapman: It seems to me that we are faced squarely with a differential diagnosis of a circumscribed, well outlined mass in the right-upper-lung field, not eroding bone, and not connected with the vascular system. In my simplicity, I would say that it boils down to a differential diagnosis between one of two diseases: gumma or malignant tumor of some type. From the clinical course and what happened to the patient I assume that the previous group of physicians in charge of him considered that the chance of a malignant tumor was greater than that of syphilis and advised operation. However, my reasoning, now that it is all over, is somewhat different. I think the weight of evidence rather favors syphilis of the lung and not a malignant lesion. Of course it could have been a malignant melanoma. We know that metastases occur years after the eye is originally enucleated. I think that we have to accept the other clinical signs and evidence of active syphilis. I would point out also that certain negative signs favor this as well. The absence of symptoms in this man, notably the lack of symptoms referable to the lungs, and the fact that cytologic smears failed to show cancer cells are against cancer. As you know, syphilis of the lung is extraordinarily rare. We seldom see it here. In a large autopsy series, 2800 I believe, Osler* found only 12 cases of syphilis of the lung. It is not too uncommon in the congenital form in the infant, but in adults it is rare. Cases have been described that fall into three categories: syphilitic pneumonitis with a stenosing lesion of the bronchus, a fibrosing lesion within the lung that can simulate tuberculosis often to the point of cavity formation and the single gummatous form that may or may not have cavitation within it from necrosis. I cannot help feeling that this patient had syphilis, which was not thoroughly treated, that he had syphilitic heart disease, with aortic regurgitation and syphilitic aortitis, and that this lesion in the chest could perfectly well have been syphilis.

The physician obviously was looking for other sources. Hypernephroma is a possibility. I remember a patient who had a lymphoma removed four or five years before he came back with a single lesion in the lung. He did not have syphilis. I decided it was metastatic; the original lesion had been removed previously. He did nicely for a month but finally died with metastases in the brain.

I wonder why the clinicians did not try antisyphilitic treatment. If it had been syphilis, it should have responded to iodides, arsphenamine or mercury. I do not know whether this was a recent case, but it seems that such a program of treatment should have been tried before operation.

A Physician: Do you think it could have been a tuberculoma, in which case the iodides would not be used?

Dr. Chapman: No; I do not. I thought of tuberculosis, but the patient had no fever, no elevated white-cell count, and no mention of the tuberculin test, and I cannot believe that it entered the minds of those taking care of him. I think they thought so strongly of its being a malignant tumor that they went ahead and removed it. But I think in view of the evidence of syphilis in the heart that it could have been a late manifestation of the disease. I do not know how I can arrive at a better diagnosis than one of those two. I cannot believe that it was pulmonary infarction. He had injection treatment for "calf pains." Did he have thromboembolic disease throwing off an embolus? I have never seen an infarct in a lung look like that, so I exclude embolic disease in the lung. Failure of progression of symptoms is against the diagnosis of cancer.

*Osler, W. *Principles and Practice of Medicine.* Fifteenth edition. 1498 pp. New York and London: D. Appleton-Century Co., 1944. P. 407.

Dr. F. Dennette Adams: In my opinion, this lesion was too well defined in outline to be syphilitic. Syphilis of the lung is rare. This lesion was so typical of tumor in its appearance that I should definitely make a diagnosis of a metastatic lesion from the original disease of the eye even at this late date. The syphilis was probably purely incidental. Dr. Wyman has just whispered in my ear that from the x-ray standpoint it could also have been a bronchiogenic carcinoma. I want to ask him a question: Does he believe that a bronchiogenic carcinoma of that size could have developed without any pulmonary symptoms or signs?

Dr. Wyman: We followed a patient with proved bronchiogenic carcinoma in the Thoracic Clinic for five years. The lesion was in the left lower lobe posteriorly, close to the chest wall, and sharply defined. It was thought to be inoperable metastatic carcinoma for a long time. This lesion was observed and filmed every few months, and during this entire time it grew very slowly and was symptomless.

From the x-ray point of view this lesion is consistent with metastatic disease or bronchiogenic carcinoma. I would not guess melanoma unless I knew about the eye. It is also quite typical of a hypernephroma.

Dr. Chapman: Would you think that it would occlude the bronchus and produce signs?

Dr. David G. Freiman: Adenocarcinomas of the bronchus, usually seen in the peripheral portions of the lung, involve the smaller bronchial radicles and often give no clinical evidence of occlusion.

Dr. Chapman: I do not see how the clinician could make a diagnosis except after an adequate trial of antisyphilitic treatment.

Dr. Adams: In the presence of aortic disease, however, one has to go slowly with antisyphilitic treatment. One might not want to wait so long to find out. I believe operation was the correct procedure and that metastatic disease of the lung is the correct diagnosis.

Clinical Diagnosis

Malignant tumor, metastatic?, primary?

Dr. Chapman's Diagnoses

Syphilis of the lung.

Melanotic sarcoma, metastatic?

Anatomical Diagnosis

Metastatic malignant melanoma of lung.

Pathological Discussion

Dr. Freiman: The operation performed was a lobectomy. We received the right upper and right middle lobes of the lung, and in the right upper lobe there was an apparently encapsulated tumor nodule, 5 cm. in diameter. The outer portion was pale, and the central portion quite black. On section this proved to be a typical metastatic malignant melanoma. We were able to obtain a section of the eye previously removed, and this showed a tumor identical in appearance with that in the lung. As has been noted, the appearance of such metastases may be long delayed and intervals of ten to fifteen years have been described following enucleation of the involved eye.

A Physician: Is the metastasis usually single?

Dr. Freiman: Metastases may be single or widely disseminated.

Dr. J. Gordon Scannell: Although a syphilitic lesion of the lung was considered preoperatively, we felt that the evidence for tumor that had increased during the past year was convincing. On seeing the patient one could not help thinking that this might have been a variation of the classic theme of a glass eye and a lump in the abdomen.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
and
THE NEW HAMPSHIRE MEDICAL SOCIETY

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MATERIAL should be received not later than noon on Thursday, three weeks before date of publication.

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ALLEGED PENICILLIN-RESISTANT GONORRHEA

AFTER a few years of the widespread and successful use of the sulfonamides in the treatment of acute gonorrhea, it was recognized by many observers that an increasing proportion of cases failed to respond to these drugs. Thus, during the year 1941, the late Oscar F. Cox[1] obtained unquestionable sulfonamide cures in 70 per cent of all male patients admitted to the Boston Dispensary with active gonococcal infections, whereas of similar cases admitted during 1944, clean-cut sulfonamide cures occurred in only 28 per cent, a complete reversal of the 1941 figure. Laboratory data in these cases indicated that the failures resulted from the resistance of the organisms and not from any change in the host. An increase in the prevalence of sulfonamide-resistant strains of *Neisseria gonorrhoeae* from 15 to 59 per cent in fifteen months was observed in Glynn County, Georgia, after the extensive use of the sulfonamides as a part of a special program for the control of gonorrhea.[2]

In Sweden, similar results were recorded in the same period. Seeberg,[3] in a report on 3428 cases of uncomplicated acute gonorrhea, mostly in males, observed that recurrences of infections after a single intensive course of sulfathiazole rose from 15 per cent early in 1941 to between 70 and 80 per cent at the end of 1943 and early in 1944. In women, the comparable failure rate was 30 per cent early in 1943 and 70 per cent at the end of the same year.

Several laboratory studies[2, 4-6] have indicated that there is a fairly close correlation between the in vitro susceptibility of gonococci to sulfonamides and the clinical response of the patients to these drugs.

The gonococcus is one of the most susceptible organisms to the action of penicillin. The sensitivity of different strains of this organism — that is, the concentration of penicillin required to inhibit growth in the test tube — has varied somewhat depending on the methods used. The great majority of strains have been found by most workers to be completely inhibited by penicillin in concentrations well below 0.1 units per cubic centimeter and usually below 0.02 units per cubic centimeter.[7-9] Sulfonamide-susceptible and sulfonamide-resistant strains are equally sensitive to penicillin.[7, 10] In vitro, it is possible to enhance the resistance of the gonococcus to penicillin, but apparently this is not accomplished easily and the limit is soon reached at a moderate level even under optimum conditions. Thus, Miller and Bohnhoff[11] succeeded in raising the resistance of one strain so that it grew in 7.7 units per cubic centimeter by repeated transfers in penicillin-containing mediums and also caused the same organism to grow in 21 units per cubic centimeter by making alternate transfers in penicillin-free mediums. The maximum concentration of penicillin in which Bahn, Ackerman and Carpenter[12] got their strains of gonococci to grow in vitro was 2 units per cubic centimeter.

With the almost universal use of penicillin in the treatment of gonococcal infections, it was expected that penicillin-resistant gonococci would

sooner or later become disseminated. This has not yet been observed on any large scale, but cases of gonorrhea that are clinically resistant to treatment with even large doses of penicillin have been reported. Thus, Pulaski[13] reported 9 cases of penicillin-resistant gonorrhea successfully treated with streptomycin. The bacteriologic observations in these cases, however, were inadequate since they were mostly controlled by smears and the identity of the organisms was not checked by cultural methods.

Franks[14] reported 4 cases successfully treated with penicillin, sulfonamides and fever therapy after repeated large doses of penicillin had failed. The organisms in these 4 cases were tested by a method in which 2 drops of penicillin solution, each containing 400 units, were put into a glass cylinder within a chocolate-agar plate that was seeded with the organisms, and no zone of inhibition of growth was noted. However, no data concerning control cultures were given, and it is not known if any of the penicillin actually diffused into the agar. If the author's interpretation is correct, his findings indicate that these 4 strains were resistant to approximately 8000 units per cubic centimeter. This is extremely unlikely, and the findings can be interpreted as probably due to the result of an error either in the identity of the strains or in the determination of their sensitivity.

In another study by Duemling and Horton,[15] 24 cases of penicillin-resistant gonorrhea were presented in which the organisms were tested by a "gutter-strip" blood-agar plate or similar method. The gonococci were said to be resistant to 5 units of penicillin per cubic centimeter, and in 1 case to 20 units. Interestingly enough, in 4 out of 5 cases in which the organism was retested after a lapse of five to nine days, during which the patient was treated with sulfonamides, the organism had lost its penicillin resistance. Treatment with sulfathiazole or sulfadiazine and then with penicillin resulted in a complete bacteriologic cure in these 24 cases. In this instance also, the results of the sensitivity tests of control strains from cases responding to the usual course of penicillin treatment are not given nor are there complete details concerning the identity of the strains of gonococci. The findings in these and similar reports are therefore open to question, particularly because of the great discrepancy in the quantitative estimation of sensitivity in view of the comparative difficulty of experimentally inducing high degrees of resistance in authentic strains of gonococci.

Three recent reports shed further light on the validity of the bacteriologic findings and on the interpretations in the alleged cases of penicillin-resistant gonorrhea. Parkhurst, Harb and Cannefax,[16] in an attempt to study such cases, deliberately accepted cases of alleged penicillin-resistant gonorrhea for treatment at the Hot Springs Medical Center. In addition, they invited the Arkansas Board of Health to refer all cases of penicillin-resistant gonorrhea to them from the local health units. In a study of over 3000 cases in males and females, including those referred as penicillin-resistant cases, they did not encounter a single case in which adequate penicillin dosage did not render the patient culturally free of the gonococcus. They believed that they had good reason to question the reliability of the diagnosis of penicillin-resistant gonorrhea based only on the clinical response and on findings in bacteriologic smears. They also believed that adequate cultural methods, including tests of the biochemical reactions and penicillin sensitivity of the organism, should be carried out before a case was diagnosed as penicillin-resistant gonorrhea. They were firmly convinced that the urethral discharges that occurred after penicillin treatment were the result of nongonococcal or nonspecific infections.

Hughes and Carpenter[17] studied 216 soldiers referred to them from the Pacific Theater and from the Zone of the Interior as penicillin-resistant cases of gonorrhea. They found 86 of these cases to be completely asymptomatic, and only 117, or 56 per cent, had any urethral exudate. Bacteriologic studies of the latter cases revealed that only 19, or 9 per cent, were positive for a gonococcus, 16 by culture of the anterior urethral discharge and 3 only by smears. Cultures of the latter 3 and of the urinary sediments of all 19 were negative for gonococcus. The predominant organism in these cases was an alpha streptococcus in 41, a hemolytic or anhemolytic staphylococcus in 51 and miscellaneous organisms in some of the others. Only 6 of the gonococcus cultures could be main-

tained satisfactorily for sensitivity tests. These were all found to be sensitive to concentrations ranging from 0.01 to 0.08 units, a range similar to that usually reported by others as already noted. Treatment of the 19 cases with a single dose of 300,000 units of calcium penicillin in beeswax and peanut oil resulted in complete clearing of the exudate in twenty-four to seventy-two hours in 14 cases. The remaining 5 patients showed no improvement in twenty-four hours, but they were rendered completely asymptomatic in another forty-eight hours after a second dose of the same amount of penicillin. These authors concluded that penicillin-resistant gonorrheal urethritis is usually nongonococcal urethritis erroneously diagnosed because of unsatisfactory bacteriologic methods.

Finally, Hawks and Greey[18] tested 330 strains of gonococci — 64 from the prepenicillin days and the rest from recent cases. The sensitivity of the strains in both groups was the same, all were inhibited by 0.06 units of penicillin, or less, per cubic centimeter.

Cases of acute gonorrhea may respond to streptomycin in moderate doses.[13, 19] It is very likely, however, that many of the cases that have been considered clinically to be penicillin-resistant gonorrhea, particularly the uncomplicated cases of urethritis that responded promptly to streptomycin, are actually cases of nongonococcal infection in which the organism is susceptible to streptomycin. It is of considerable theoretical interest as well as of practical importance to determine for certain whether or not there are any penicillin-resistant strains of gonococci prevalent in the community and whether or not their numbers are increasing. Physicians who encounter cases of infection in which the presence of such penicillin-resistant gonococci is suspected should make every effort to obtain proper cultures or see that such cultures are made in laboratories where there is sufficient interest and where facilities are available for the proper identification of the strains and the determination of their sensitivity to the antibiotic.

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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

The American Association for the Advancement of Science will hold its Centennial Meeting in Washington, D. C., September 13 to 17, 1948. The morning programs will consist of technical symposiums on important scientific problems; the evening sessions, after the first evening, will be devoted to semipopular lectures that will be open to the general public. Two addresses will be given at the first evening meeting, by the President of the United States and by the retiring president of the Association, Dr. Harlow Shapley.

A hundred years ago, on September 20, 1848, the first meeting of this distinguished society was called to order in the library room of the Academy of Natural Sciences of Philadelphia by Professor William B. Rogers, of Virginia. Professor Walter R. Johnson, of Washington, served as secretary, and with the assistance of a special committee collected the proceedings of the sessions in a volume of 156 pages.

The origin and the organization of the Association were duly recorded: " 'In conformity with a resolution of the Association of American Geologists and Naturalists,' adopted during its session at Boston in September, 1847, that body agreed to resolve itself into the American Association for the Advancement of Science . . . ."

The first president of the Association, William C. Redfield, Esq., of New York, assumed office that afternoon. The first paper of the meeting was forthwith read by Peter A. Brown, L.L.D., on *Some Notice of the Fossil Cephalopodes Belemnosepia, Long Known by the Name of 'Belemnite,' and of the Diphosphate of Iron, called 'Mullicite,' Found Together at Mullica Hill.*

The *Journal* wishes long life and continued prosperity to the American Association for the Advancement of Science. The next hundred years should be easier.

BARUCH COMMITTEE REPORT

CONTINUED progress in the development of physical medicine and facilities for the rehabilitation of the sick and disabled is indicated in the annual report of the Baruch Committee on Physical Medicine, recently released. The Committee was founded by Mr. Bernard M. Baruch in 1944 in memory of his father, Dr. Simon Baruch, a pioneer in physical medicine.

According to this report, the committee has already achieved its major objectives of increasing the number of physicians trained to teach and use the methods of physical medicine, of providing facilities for more extensive research in physical medicine and for "insuring the proper use of physical medicine in relation to wartime rehabilitation and peacetime physical preparedness."

There are now, according to Dr. Frank H. Krusen, director of the Committee and director of physical medicine at the Mayo Foundation, approximately 150 communities in the country that have or are planning civilian rehabilitation programs. Already many of the rehabilitation services in Veterans Administration, Army and Navy hospitals are directed by physicians whose training the Baruch Committee sponsored.

As further evidence of an increased awareness of the need of opportunities for rehabilitation, the seventy residencies and fellowships now available at thirty-four medical centers may be compared with the five such appointments available five years ago. Today sixty medical schools instead of the thirty that existed before the Committee was organized offer instruction in physical medicine.

The need for an organized rehabilitation program has long existed. Four years of war increased the need and conditioned the public in its favor. The labors of the Baruch Committee and the generosity of its founder have provided much of the actual power for accomplishment.

STRANGE HOST

AN interesting sidelight on the part that wild life may play in man's destiny has been exposed by Thorborg and his associates[1] and made the subject of an annotation in the Lancet.[2]

It appears that in May, 1947, the State Serum Institute in Copenhagen was made aware of a mysterious epidemic that had broken out in Greenland. During the previous five months about 300 cases of an acute and distressing malady had occurred, with a 10 per cent mortality. The disease usually began gradually although sometimes the onset was acute. Progressive lassitude became evident with headache, pains in limbs and trunk, and fever, slight at first, then rising to considerable heights. Gastrointestinal symptoms developed, and edema of the face, limbs or entire body was an almost constant feature. The cases of sudden death were apparently the result of myocardial failure.

Trichiniasis had never been known to occur in Greenland, but Thorborg, who was sent to investigate the epidemic, found eosinophilia, positive cutaneous reactions to trichina antigen, positive serologic tests on blood samples and encapsulated trichina larvae in the muscles of a patient who had died of the disease after a three months' illness.

Pork was not involved in this initial outbreak of trichiniasis, and only a few of the patients had eaten dog meat within a month of the onset of symptoms. The only common factor was the synchronization of the epidemic with the walrus-hunting season

and the consequent consumption of walrus meat, although there was reason for suspecting also the white whale.

Bizarre phenomena still occur in nature, and one is repeatedly reminded that God moves in a mysterious way in the performance of His wonders. There is no evidence that the walruses of Greenland have ever been implicated in the fantastic social and gastronomic relations described by Carroll,[3] but one may wonder if the oysters on which they might have fed had had their prescribed veterinary inspection.[4]

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4. Editorial. Through the looking glass. *New Eng. J. Med.* **239**:240, 1948.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

RHEUMATIC-FEVER FELLOWSHIPS

The United States Children's Bureau has made available through the Massachusetts Department of Public Health and Harvard Medical School two fellowships in rheumatic fever at the House of the Good Samaritan of the Children's Medical Center, Boston, for the year 1948, beginning immediately.

Trainees should be interested in working eventually in the field of rheumatic fever in public health or in teaching, rather than in private practice.

Work under these fellowships probably will be acceptable for credit by the Board of Internal Medicine or the Board of Pediatrics.

Application should be made to Dr. Benedict F. Massell at the House of the Good Samaritan, 25 Binney Street, Boston 15, or by telephone call to BEacon 2-3002.

ADMISSION OF CRIPPLED CHILDREN TO LAKEVILLE STATE SANATORIUM

The Department of Public Health announces that under the provisions of Chapter 412, Acts of 1948, it has been authorized to admit to Lakeville State Sanatorium certain crippled children provided that they have been residents of the Commonwealth for at least twelve months preceding the date of application for admission. Prior to the passage of this act Lakeville Sanatorium had been authorized to admit only patients with extrapulmonary forms of tuberculosis and persons crippled with infantile paralysis.

Because of the steady decline in extrapulmonary forms of tuberculosis, beds are now available for the treatment of other orthopedic conditions, and this act will make these facilities available for indigent children for whom the Commonwealth cannot provide necessary treatment in general hospitals.

Crippling conditions, including cerebrospastic palsy, spina bifida, clubfoot, congenital dislocations and deformities, obstetric paralysis, osteomyelitis, osteochondritis, epiphysitis and scoliosis, are considered suitable for treatment at Lakeville.

Applications for admissions of crippled children may be filed by any registered physician with the Massachusetts Department of Public Health, Room 546, State House, Boston.

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JULY, 1948

Résumé

Diseases	July 1948	July 1947	Seven-Year Median
Chancroid	4	2	2*
Chicken pox	619	664	516
Diphtheria	15	19	14
Dog bite	1517	1316	1229
Dysentery, bacillary	9	11	11
German measles	61	52	116
Gonorrhea	284	352	356
Granuloma inguinale	0	0	1*
Lymphogranuloma venereum	0	0	2*
Malaria	4	15	15
Measles	2462	616	1159
Meningitis, meningococcal	5	7	13
Meningitis, Pfeiffer-bacillus	4	1	2
Meningitis, pneumococcal	2	2	2†
Meningitis, staphylococcal	0	0	0†
Meningitis, streptococcal	0	0	0†
Meningitis, other forms	2	0	0†
Meningitis, undetermined	6	3	4†
Mumps	787	347	434
Pneumonia, lobar	124	107	100
Poliomyelitis	9	21	11
Salmonellosis	2	13	11
Scarlet fever	269	120	241
Syphilis	225	216	363
Tuberculosis, pulmonary	271	218	218
Tuberculosis, other forms	19	12	17
Typhoid fever	4	1	4
Undulant fever	5	6	4
Whooping cough	130	551	562

*Four-year median.

†Six-year median.

Comment

Diseases with an incidence above the seven-year median were chicken pox, diphtheria, measles, mumps, lobar pneumonia, scarlet fever and undulant fever.

Diseases with an incidence below the seven-year median were bacillary dysentery, German measles, poliomyelitis and whooping cough.

The apparent increase in lobar pneumonia was due to delayed hospital reporting.

July had the highest incidence for mumps since 1915; whooping cough showed the lowest incidence since 1915.

Geographical Distribution of Certain Diseases

Actinomycosis was reported from: Brockton, 1; total, 1.

Diphtheria was reported from: Athol, 1; Berkley, 2; Boston, 8; Braintree, 1; Cambridge, 1; Revere, 1; Weymouth, 1; total, 15.

Dysentery, bacillary, was reported from: Dedham, 1; Waltham, 1; Worcester, 6; Wrentham, 1; total, 9.

Encephalitis, infectious, was reported from: Hudson, 1; Milford, 1; Worcester, 1; total, 3.

Lymphocytic choriomeningitis was reported from: Cambridge, 1; total, 1.

Malaria was reported from: Greenfield, 1; Medford, 1; Revere, 1; Springfield, 1; total, 4.

Meningitis, meningococcal, was reported from: Boston, 2; Brookline, 1; Cambridge, 1; Winchester, 1; total, 5.

Meningitis, Pfeiffer-bacillus, was reported from: East Bridgewater, 1; Marlboro, 1; Revere, 1; Salem, 1; total, 4.

Meningitis, pneumococcal, was reported from: Boston, 1; Worcester, 1; total, 2.

Meningitis, other forms, was reported from: Boston, 2; total, 2.

Meningitis, undetermined, was reported from: Arlington, 1; Cambridge, 1; Leominster, 2; Springfield, 1; Westfield, 1; total, 6.

Poliomyelitis was reported from: Boston, 2; Cambridge, 1; Dartmouth, 1; Great Barrington, 1; Natick, 1; Waltham, 1; Westford, 1; Worcester, 1; total, 9.

Salmonellosis was reported from: Medford, 1; Worcester, 1; total, 2.

Septic sore throat was reported from: Medford, 1; total, 1.

Trichinosis was reported from: Boston, 1; Cambridge, 1; Lexington, 1; total, 3.

Typhoid fever was reported from: Chelmsford, 1; Dartmouth, 1; Gloucester, 1; Melrose, 1; total, 4.

Undulant fever was reported from: Boston, 1; Cambridge, 1; Chesterfield, 1; Dudley, 1; Webster, 1; total, 5.

MISCELLANY

NATIONAL HEART INSTITUTE

Establishment of the National Heart Institute as one of the National Institutes of Health in the United States Public Health Service has been announced by Oscar R. Ewing, federal security administrator.

Concurrently, Surgeon General Leonard A. Scheele, United States Public Health Service, has announced the appointment of Dr. Cassius J. Van Slyke as director of the National Heart Institute, under the general supervision of Assistant Surgeon R. E. Dyer, director of the National Institutes of Health. In addition, Dr. Van Slyke will be directly responsible to the Surgeon General for co-ordination of all heart-disease activities in the Public Health Service, representing the Service in maintaining relations with professional societies, voluntary agencies and other civic groups that are interested in the progress of the heart-disease program.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Factors Regulating Blood Pressure: Transactions of the first conference, April 24-25, 1947, New York. Edited by B. W. Zweifach and Ephraim Shorr, Department of Medicine, Cornell University Medical College, New York. New York: Josiah Macy, Jr., Foundation, 1947. $1.90.

This new conference in the Josiah Macy, Jr., Foundation series of conferences was participated in by nineteen authorities from Boston, New York City and other parts of the country. The papers and discussions deal with the various aspects of the subject. The publication should be in all medical libraries.

Treatment in General Practice. By Harry Beckman, M.D., professor of pharmacology, Marquette University School of Medicine, Milwaukee. Sixth edition. 8°, cloth, 1129 pp. Philadelphia: W. B. Saunders Company, 1948. $11.50.

Dr. Beckman has revised thoroughly this last edition of his standard work on treatment. Many subjects have been completely rewritten, and much material has been added, including balantidiasis, coccidiosis, Colorado tick fever, creeping eruption, geotrichosis, Listerellosis, Loeffler's syndrome, melioidosis, mite infestation, moniliasis, new anemias, nonmeningococcal meningitides, North Queensland tick typhus, pulmonary aspergillosis, Reiter's syndrome, rickettsialpox, thrombosis and embolism and the management of penicillin reactions. A long bibliography of sixty-five pages is appended to the text, and a comprehensive index concludes the volume. The text is well printed with a good type, on good light paper. The work is recommended for all medical libraries and for the collections of practicing physicians.

La penicillina in chirurgia per infiltrazione locale massiva. By Sante Ciancarelli, chirurgo degli Ospedali di Roma — clin. mal. infettive (Dir. G. Caronia). 4°, paper, 47 pp. Roma: Luigi Pozzi, 1948.

The author of this small monograph has used his method of local massive infiltration of penicillin in surgical conditions for three years with good results. He describes his method of administration and the dosage used. He has treated osteomyelitis, suppuration of the hand, empyema of the pleura, lung abscess, mastitis, tonsillitis, lymphadenitis, abscesses, peritonitis, cerebral abscess and Ludwig's angina. The text is in Italian. The pamphlet is well printed, with a good type on good paper.

Conference on Liver Injury: Transactions of the fifth meeting September 26-27, 1946, New York. 8°, paper, 128 pp. $2.25. *Liver Injury: Transactions of the sixth conference May 1 and 2, 1947, New York.* 8°, paper, 74 pp. $2.00. Edited by F. W. Hoffbauer, M.D., Mayo Foundation, Rochester, Minn. New York: Josiah Macy, Jr., Foundation, 1947.

The fifth conference on liver injury discussed the relation of dietary factors to chemical liver injury, hepatic functional impairment from vitamin deficiency, liver function, chronic hepatitis and therapy in liver diseases, the sixth considered cirrhosis, the hepatorenal syndrome, chromatography in the study of liver disease and massive hepatic necrosis. These two volumes and the set should be in all medical libraries.

Diseases of the Skin. By Oliver S. Ormsby, M.D., attending dermatologist to the Presbyterian Hospital of Chicago; and Hamilton Montgomery, M.D., M.S., associate professor of dermatology and syphilology, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota, Rochester. Seventh edition, thoroughly revised. 8°, cloth, 1462 pp., with 683 figures and 11 plates. Philadelphia: Lea & Febiger, 1948. $18.00.

This standard authoritative text has been thoroughly revised by the incorporation of new material and the deletion of obsolete material. The additions include a number of new diseases not described in the previous edition and new methods of treatment of syphilis and other diseases with penicillin and other antibiotics. To keep the volume within bounds some chapters have been condensed and some of the text printed in small type. Ninety figures and eleven color illustrations have been added to the text. References have been limited and printed as footnotes on the appropriate pages. A good index concludes the volume. The book is well published and is recommended for all medical libraries and to dermatologists and physicians interested in diseases of the skin.

Mental Health in Modern Society. By Thomas A. C. Rennie, M.D., associate professor of psychiatry, Cornell University Medical College, and director, Division on Rehabilitation, National Committee for Mental Hygiene; and Luther E. Woodward, Ph.D., field consultant, Division on Rehabilitation, National Committee for Mental Hygiene. 8°, cloth, 424 pp. New York: The Commonwealth Fund, 1948. $4.00.

The authors have based their book on actual work in the field of mental health, in psychiatry and psychiatric social work in the New York Hospital Rehabilitation Clinic for Psychiatrically Disabled Veterans and in field work in communities and states and in the sharing of experience with leaders in the various governmental and public services. The work is divided into three parts: lessons from the war period, in four chapters; post-emergency problems in mental health, in one chapter; and sources of help in treatment and prevention, in eight chapters. The work is so comprehensive that an analytical review is excluded because of space limitations that will permit only an indication of the contents. The war period is discussed under the headings of mental-health services in the armed forces, emergency measures for aiding veteran-civilian adjustment, and psychiatric disabilities of war: dynamics and motivation, principles, methods and results of treatment. The second part considers the continuing mental-health problems and needs, including problems of the wounded and veterans with psychiatric disabilities, the effect of war on the civilian population, research and problems relating to more and better treatment of the mentally ill. The third part discusses the

possible contributions to treatment and to constructive mental health that can be made by family physicians, social workers and psychologists and by the church, industry, community organizations and the Government. The final chapter presents a summary and prospect: the individual and society. The objective of the book has been to show that mental and emotional ill health is a reaction of personality to the multiple stresses of the total environment, whether the stresses be in external environment, or in the patient's own complicated emotional imbalances. The authors state that mental health cannot be developed in a social vacuum and that to promote positive mental health will require the co-operation and help of many individuals and groups. The material is well organized, and the text is well written. A list of references is appended to each chapter. A good index concludes the volume. The publishing is excellent in every way. The printing is well done with a good large type on good nonglare paper. It is a pleasure to read the book. The book is recommended for all medical, social, public-health and general libraries and to all persons interested in the subject.

Psychobiology and Psychiatry: A textbook of normal and abnormal human behavior. By Wendell Muncie, M.D., practicing psychiatrist, chairman, Medical Advisory Board, Seton Institute, Baltimore, and associate professor of psychiatry, Johns Hopkins University, and consultant in psychiatry, U. S. V. A. Second edition. 8°, cloth, 620 pp., with 70 illustrations. St. Louis: The C. V. Mosby Company, 1948. $9.00.

This second edition has been extensively edited by the author in the light of his experience gained in private practice since the publication of the first edition in 1939. The textbook is based on the teaching of psychiatry at Johns Hopkins University School of Medicine. The historical appendixes of the first edition have been omitted from this edition. A list of selected references is appended to each chapter. A good index concludes the volume. The publishing is well done. The work should be in all collections on psychiatry.

Encyclopedia of Medical Sources. By Emerson C. Kelly, M.D., associate professor of surgery, Albany Medical College, and attending surgeon, Albany Hospital. 8°, cloth, 476 pp. Baltimore: The Williams and Wilkins Company, 1948. $7.50.

This book is essentially a medical biographic dictionary, in which the fundamental contributions of the persons listed are emphasized, and extensive biographic data omitted. Birth and death dates and domicile are given. Dr. Kelly consulted about 95 per cent of the original publications, a very large coverage, in the interest of accuracy. The names are listed alphabetically, and a comprehensive subject index concludes the volume. The index refers to names and not pages throughout the text. The book is recommended as an essential reference work for all medical and general libraries and to all medical historians.

Clinical Diagnosis by Laboratory Methods: A working manual of clinical pathology. By James C. Todd, Ph.B., M.D.; and Arthur H. Sanford, A.M., M.D., professor of clinical pathology, Mayo Foundation, University of Minnesota, and senior consultant, Division of Clinical Laboratories, The Mayo Clinic. With the collaboration of George G. Stilwell, M.D., Division of Clinical Laboratories, The Mayo Clinic. Eleventh edition. 8°, cloth, 954 pp., with 397 illustrations. Philadelphia: W. B. Saunders Company, 1948. $7.50.

This standard popular textbook was published first in 1908 and has gone through ten previous editions, the tenth being issued in 1943. The text of this eleventh edition has been completely revised, and some rearrangement has been made in the subjects. The former chapter on serodiagnostic methods has been divided into three short chapters, and the serodiagnostic tests for syphilis have been included in the second of these chapters. The material on medical mycology has been expanded into a new chapter. The illustrations have been carefully reviewed and rearranged, and new ones added, including new color plates on the blood. A list of references is appended to each chapter. A comprehensive index concludes the volume. The publishing is well done in the characteristic Saunders style. The book is recommended for all medical libraries and to the general practitioner.

Introduction to Human Physiology. By William D. Zoethout, Ph.D. 8°, cloth, 424 pp., with 138 illustrations and 4 color plates. St. Louis: The C. V. Mosby Company, 1948. $4.00.

This elementary manual is well written in a simple, lucid style, and the material is well organized. The type, printing and paper are excellent. The manual should prove of value to students and to all persons interested in the subject. It is recommended for public libraries, where it should prove useful in semipopular collections.

Clinical Studies in Psychopathology: A contribution to the aetiology of neurotic illness. By Henry V. Dicks, M.A., M.D. (Cantab.), F.R.C.P. (Lond.), Nuffield Professor of Psychiatry in the University of Leeds. Second edition. 8°, cloth, 238 pp. Baltimore: The Williams and Wilkins Company, 1947. $4.50.

The author has not made any major changes in this second edition of his small book on psychopathology, but has confined himself to making certain minor improvements. The case records remain the same as in the first edition. The author believes that psychopathology was not changed fundamentally by World War II and therefore has not felt compelled to change his point of view on the subject. Some of the subjects discussed include anxiety and obsessional states, hysteria, sexual perversions, abnormalities of sexual function and drug addictions. A good index concludes the volume. The composition and printing were done in Great Britain, accounting for the yellowish tinge in the paper. The sheets were bound in the United States. The book is essentially an English publication, reflecting the British viewpoint. The volume should be in all neurologic and psychiatric collections.

Psychotherapy: Its use and limitations. By D. Rhodes Allison, M.D., M.R.C.P.; and R. G. Gordon, M.D., D.Sc., and F.R.C.P. 12°, cloth, 160 pp. New York: Oxford University Press, 1948. $3.00. (Oxford Medical Publications.)

This semipopular manual has been written for the student, the physician and the intelligent layman. It does not describe the methods of psychotherapy but endeavors to present the subject in a broad way, pointing out to the physician and the family ways to help the patient by maintaining his morale and courage. The material is well organized and covers the field of the psychoneuroses, with chapters on the psychoses, mental deficiency and psychopathic personalities. There are chapters on the relation of rheumatism to mental illness, other psychomatic conditions and the patient's reaction to bodily disease. A good index concludes the volume. The book is well published and should prove useful to persons interested in the subject.

NOTICES

ANNOUNCEMENTS

Dr. Harrison E. Kennard announces the removal of his office to 1180 Beacon Street, Brookline, for the practice of general surgery.

Dr. Aaron Thurman announces the removal of his office to the Lister Building, 475 Commonwealth Avenue, Boston.

AMERICAN COLLEGE OF SURGEONS

As previously announced, the twenty-seventh annual Hospital Standardization Conference will be held at the Biltmore Hotel, Los Angeles, from October 18 to 22, in conjunction with the thirty-fourth annual Clinical Congress of the American College of Surgeons.

The opening session of the Clinical Congress is a joint meeting for surgeons and hospital representatives on Monday morning, October 18, at 10 o'clock, at which the president of the American College of Surgeons, Dr. Arthur W. Allen, of Boston, president-elect of the Massachusetts Medical Society, will preside and speak on "Looking Forward with Hospital Standardization."

COLLEGE OF AMERICAN PATHOLOGISTS

The Northeastern Regional Meeting of the College of American Pathologists will be held at the Massachusetts General Hospital, Boston, on September 18.

PROGRAM

8:30–9:30 a.m. Registration.
9:30–10:00 a.m. Recent Advances in Laboratory Diagnosis of Pregnancy. Stanley L. Robbins, M.D.
10:00–10:30 a.m. Hormonal Alteration of Breast Carcinoma. Ira T. Nathanson, M.D.
10:30–11:00 a.m. Practical Problems in the Rh Investigation. Louis K. Diamond, M.D.
11:00–11:30 a.m. Neuropathology: Its current methods and values. Raymond D. Adams, M.D.
11:30 a.m.–12:00 m. The Use of Photoelectric Spectrophotometry in Clinical Problems. Francis T. Hunter, M.D.
12:00 m.–12:30 p.m. The Role of the Laboratory in the Diagnosis of Tuberculosis. William Steenken, Jr., M.D.
12:30–2:00 p.m. Luncheon in Cafeteria, Massachusetts General Hospital.
2:00–2:30 p.m. Diagnostic Procedures in Virus Diseases of the Respiratory Tract. Maxwell Finland, M.D.
2:30–3:00 p.m. Diagnostic Procedures in Certain Virus Diseases of the Central Nervous System. John F. Enders, M.D.
3:00–4:00 p.m. Pathology of the Newborn. Sidney Farber, M.D.
4:00–5:00 p.m. Difficulties and Pitfalls in Interpretation of Vaginal and Pulmonary Smears by the Papanicolaou Method. Ruth M. Graham, S. B.
6:00 p.m. Fellowship.
7:00 p.m. Dinner at Hampshire House, 84 Beacon Street, Boston ($4.60 per person).
8:00 p.m. Human Sexuality. John Rock, M.D.

AMERICAN TRUDEAU SOCIETY

The Eastern Section of the American Trudeau Society will meet on October 15, 1948 at the Rutland State Sanatorium, Rutland, Massachusetts. This meeting will be among the events arranged to mark the fiftieth anniversary of the opening of the institution, the first of its kind in America.

METROPOLITAN STATE HOSPITAL

The Fourteenth Postgraduate Seminar in Neurology and Psychiatry will begin on Friday, October 1. The program will be as follows: a review course in basic neurology and psychiatry, consisting of sixty-six lectures to be held every Friday from 2 to 10 p.m. from October 1 to December 3, 1948, and from March 4 to May 20, 1949, at the Metropolitan State Hospital, 475 Trapelo Road, Waltham; a course in social and special psychiatry consisting of thirty-six lectures, to be held every Wednesday from 5:30 to 10 p.m. from October 13 to December 8, 1948, and from March 16 to May 11, 1949, at the Boston Psychopathic Hospital, 74 Fenwood Road, Boston; and a course in pediatric neuropsychiatry (child psychiatry) consisting of twenty lectures, to be held every alternate Monday from 6 to 10 p.m. from October 11 to December 6, 1948, and from March 14 to May 9, 1949, at the Walter E. Fernald State School, Waverley.

All interested graduate physicians should apply before October 1 in writing to Dr. William C. Gaebler, superintendent, Metropolitan State Hospital, Waltham.

The applicants should indicate which of the three courses of the Seminar they wish to attend. The registration is requested as a matter of courtesy to the institutions where courses are conducted and as a convenience for the registrants, who will thus be able to receive the schedules and who will be notified in time in case changes in the schedule should become necessary during the year.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS

The annual meeting of the American Society of Anesthesiologists will be held in St. Louis from November 4 to 6.

THE FOUNDATION PRIZE

The South Atlantic Association of Obstetricians and Gynecologists announces the establishment of the Foundation Prize. Authors of papers on obstetric or gynecologic subjects desiring to compete for the prize may obtain information from Dr. E. D. Colvin, secretary-treasurer, 1259 Clifton Road, N. E., Atlanta, Georgia.

COLORADO STATE MEDICAL SOCIETY

The annual meeting of the Colorado State Medical Society will be held in Glenwood Springs from September 22 to 25 (secretary, H. T. Sethman, Republic Building, Denver 2, Colorado).

INDIANA STATE MEDICAL ASSOCIATION

The annual meeting of the Indiana State Medical Association will be held in Indianapolis from October 26 to 28 (secretary, Ray E. Smith, 23 East Ohio Street, Indianapolis 4, Indiana).

KENTUCKY STATE MEDICAL ASSOCIATION

The annual meeting of the Kentucky State Medical Association will be held in Covington from September 27 to 30 (secretary, P. E. Blackerby, M.D., 620 South Third Street, Louisville 2, Kentucky).

MICHIGAN STATE MEDICAL SOCIETY

The annual meeting of the Michigan State Medical Society will be held in Detroit, September 22 to 24 (secretary, L. Fernald Foster, M.D., 2020 Olds Tower, Lansing 8, Michigan).

NEVADA STATE MEDICAL ASSOCIATION

The annual meeting of the Nevada State Medical Association will be held in Ely on September 24 and 25 (secretary, Roland W. Stahr, M.D., 118 California Avenue, Reno, Nevada).

MEDICAL SOCIETY OF VIRGINIA

The annual meeting of the Medical Society of Virginia will be held in Richmond from October 18 to 20 (secretary, Miss A. V. Edwards, 1200 East Clay Street, Richmond 19, Virginia).

WASHINGTON STATE MEDICAL ASSOCIATION

The annual meeting of the Washington State Medical Association will be held in Seattle from October 3 to 6 (secretary, John P. McVay, M.D., 327 Cobb Building, Seattle 1, Washington).

STATE MEDICAL SOCIETY OF WISCONSIN

The annual meeting of the State Medical Society of Wisconsin will he held in Milwaukee from October 4 to 6 (secretary, C. H. Crownhart, 110 East Main Street, Madison 3, Wisconsin).

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 16

FRIDAY, SEPTEMBER 17
*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.

TUESDAY, SEPTEMBER 21
*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

WEDNESDAY, SEPTEMBER 22
*12:00 m.–1:00 p.m. Clinical Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*Open to the medical profession.

SEPTEMBER 13–15. American Academy of Pediatrics. Olympic Hotel, Seattle, Washington.

SEPTEMBER 14. New England Society of Anesthesiologists. Page 316, issue of August 19.

(*Notices concluded on page xv*)